Original Article

Microarray Analysis of the Gene Expression Profile in Triethylene Glycol Dimethacrylate-treated Human Dental Pulp Cells

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ABSTRACT

Objective: Triethylene glycol dimethacrylate (TEGDMA) is an important resin monomer commonly used in the structure of dental restorative materials. Recent studies have shown that unpolymerized resin monomers may be released into the oral environment and cause harmful biological effects. We investigated changes in the gene expression profiles of TEGDMA-treated human dental pulp cells (hDPCs) following short- (1-day) and long-term (7-days) exposure. **Materials and Methods:** HDPCs were exposed to a noncytotoxic concentration of TEGDMA, and gene expression profiles were evaluated by microarray analysis. The results were confirmed by quantitative reverse-transcriptase PCR (qRT PCR). **Results:** In total, 1282 and 1319 genes (up- or down-regulated) were differentially expressed compared with control group after the 1- and 7-day incubation periods, respectively. Biological ontology-based analyses revealed that metabolic, cellular, and developmental processes constituted the largest groups of biological functional processes. qRT-PCR analysis on bone morphogenetic protein-2 (*BMP*-2), *BMP*-4, secreted protein, acidic, cysteine-rich, collagen type I alpha 1, oxidative stress-induced growth inhibitor 1, MMP3, interleukin-6, and heme oxygenase-1 genes confirmed the changes in expression observed in the microarray analysis. **Conclusions:** Our results suggest that TEGDMA can change the many functions of hDPCs through large changes in gene expression levels and complex interactions with different signaling pathways.

KEYWORDS: *Gene expression, human dental pulp cell, microarray, triethylene glycol dimethacrylate*

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INTRODUCTION

Resin monomers are widely used in dentin bonding agents and composite resins to restore teeth structures impaired by caries or fractures. With its hydrophilic structure and low molecular weight, triethylene glycol dimethacrylate (TEGDMA) is an important resin monomer and undergoes rapid polymerization after light curing. Due to its hydrophilic nature, the degradation processes and insufficient polymerization of TEGDMA cause the release of dental resin monomers into the oral environment, which can trigger hazardous biological effects on living oral tissues.[1,2] Dentin thickness and the severity of the caries lesion are important factors in determining the amount of resin monomers interacting with dental pulp tissue.[3]

Various studies have been performed to show the adverse biological effects of TEGDMA on different mammalian cells. Previous studies revealed that TEGDMA has considerable cytotoxicity against different cell types via DNA damage, caspase activation, induction of apoptotic proteins, and reactive oxygen species.[4-10] TEGDMA also influences the odontogenic differentiation capacity of dental pulp cells by decreasing the expression of mineralization-related genes.[11] TEGDMA can cause changes in the immune system by affecting cytokine

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production and the expression of surface markers that are essential for immune cells.[12,13] These findings suggest that TEGDMA interacts with living cells by influencing different biological pathways and causing adverse effects.

Recently, high-throughput procedures such as DNA microarray and RNA-seq technologies have been used to investigate the effects of high and low doses of TEGDMA on skin fibroblasts and human dental pulp cells (hDPCs), respectively.[9.11] These studies have greatly contributed to scientific knowledge regarding the basic mechanisms of action of TEGDMA, but unknown issues remain to be determined. Microarray analysis can be used to decipher the expression state of tens of thousands of genes in a single experiment. Microarrays provide an opportunity to explore the effects of various materials and allow researchers to evaluate the overall state of a cell. In addition, gene ontology databases contribute to the understanding of predominant biological processes, pathways, and functional regulatory networks from the microarray data.

In the present study, we tested the hypothesis that an increase in the exposure time of hDPCs to TEGDMA may differentially alter the gene expression profile of hDPCs. Thus, hDPCs and high-throughput DNA microarray analysis were used to test whether TEGDMA changed gene expression profiles after 1- and 7-day exposure periods.

Materials and Methods

Cell culture

This study was approved by the local Ethics Committee. Dental pulp tissues were obtained from the molars of healthy patients undergoing orthodontic treatments. Extracted molars were kept in phosphate-buffered saline solution (Biological Industries, Kibbutz Beit Haemek, Israel) containing 100 U/mL penicillin and 100 µg/mL streptomycin (Biological Industries) to eliminate bacterial contamination. After transferring to the laboratory, extracted molars were cut horizontally 1 mm below the cementoenamel junction. The pulp tissues were gently separated from the crown and root and placed in a 100-mm Petri dish. Pulp tissues were cut into small pieces with a blade and cultured in Dulbecco's Modified Eagle's Medium (DMEM; Biological Industries) containing 10% fetal bovine serum (FBS; Biological Industries), 100 U/mL penicillin, and 100 µg/mL streptomycin (Biological Industries). Tissue cultures were maintained in a humidified atmosphere of 5% CO_2 at 37°C. Cells from the fifth passage were used for subsequent experiments and cultured for 24 h before analysis.

XTT assay

The XTT assay was used to determine the noncytotoxic dose of TEGDMA. The XTT assay is useful for determining cellular proliferation and viability by spectrophotometric quantification. The assay is used to measure cell proliferation in response to growth factors, cytokines, and nutrients based on the conversion of the yellow tetrazolium salt 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide) to an orange formazan dye by metabolically active and viable cells. Cells (100 µL/well) were seeded into 96-well plates at 2×10^4 per well and incubated for 24 h in a humidified atmosphere of 5% CO_2 at 37°C. Then, three groups were prepared: 0.3 mm TEGDMA, 1 mm TEGDMA, and 3 mm TEGDMA. TEGDMA was purchased from Sigma-Aldrich (Sigma Chemical Company, St. Louis, MO, USA). Untreated cell cultures were used as control. The cell cultures were exposed to serial dilutions of the test materials. After an incubation period of 7 days, 50 µL (0.3 mg/mL) of XTT labeling mixture (Cell Proliferation Kit II; Roche, Mannheim, Germany) was added to each well, followed by incubation for 4 h in a humidified atmosphere of 5% CO_2 at 37°C. The absorbances of the metabolized media were measured at 450 nm using a microplate reader (ELX800BKT, Bio-Tek Instruments, USA). Cell viabilities of the test groups were calculated as a percentage of the control group. Each experimental group consisted of nine samples.

Microarray analysis

The TEGDMA concentration to be used for microarray analysis was decided by determining where it exhibited significantly different ($P < 0.05$) but higher cell viability (>90%) after 7 days. Thus, 1 mm TEGDMA was selected as the experimental dosage. hDPCs were seeded into 12-well plates at 1×10^6 per well and incubated for 24 h in a humidified atmosphere of 5% CO_2 at 37°C. Cells were pooled 1; 7 days after, 1 mm TEGDMA was applied. Cell pooling was conducted from 3 wells of each group. Wells without TEGDMA were also cultured for 1 and 7 days, and untreated hDPCs were used as controls. Each experimental group consisted of four samples.

Total RNA from hDPCs was extracted using the RNeasy Mini Kit (Qiagen, Valencia, CA) according to the manufacturer's instructions. RNA purity and integrity were quantified using a p360 Nanophotometer (Implen, Germany). The microarray analysis was performed using the GeneChip 3 IVT Express Kit (Affymetrix, USA). Briefly, total RNA was subjected to reverse transcription (first-strand cDNA synthesis), converted into double-strand cDNA, *in vitro* transcription, purification, and fragmentation. The samples were hybridized onto the GeneChip PrimeView Human Gene

Expression Array (Affymetrix), which covers more than 36,000 transcripts and variants. After hybridization for 16 h at 45°C, the arrays were washed and then scanned to obtain quantitative gene expression levels.

Data were analyzed using the Expression Console and Transcriptome Analysis Console/Partek Genomic Suite. Raw data were normalized by the robust multiarray average algorithm. Array data were filtered by detection $P < 0.05$. A comparative analysis between each sample was carried out using fold-change data. Biological, ontology-based analyses were conducted using the PANTHER database (http://www.pantherdb.org).

Quantitative real-time PCR (qRT-PCR) analysis

To confirm the results obtained from the microarray experiments, qRT-PCR was performed. Bone morphogenetic protein-2 (*BMP*-2), *BMP*-4, secreted protein, acidic, cysteine-rich (*SPARC*), collagen type I alpha 1 (*COL1A1*), oxidative stress-induced growth inhibitor 1 (*OSGIN1*), matrix metallopeptidase-3 (*MMP-3*), interleukin-6 (*IL-6*), and heme oxygenase-1 (*HMOX1*) genes were chosen due to their relationship with mineralization, bone formation, extracellular matrix (ECM) formation, DNA damage, oxidative stress, apoptosis, and inflammation, respectively. β-actin (ACTB) was used as a housekeeping gene to normalize RNA expression. qRT-PCR analyses were conducted using the total RNA samples previously described for the microarray analyses. cDNA was synthesized from 25 ng of total RNA using the Transcriptor High Fidelity cDNA Synthesis Kit (Roche). The cDNA obtained was used as a template for PCR. The target cDNA was then amplified using specific primer pairs [Table 1]. qRT-PCR was performed using the Faststart Essential DNA Green Master (Roche) and a LightCycler Nano Instrument (Roche).

The 20-μL reaction mixture consisted of 5 μL cDNA, 4 μL water, 10 μL × 2 master mix buffer, and a final concentration of 0.25 pmol/μL of each primer. qRT-PCR conditions included an initial denaturation step at 95°C for 10 min, followed by 45 cycles at 95°C for 10 s, 60°C for 10 s, and 72°C for 10 s. The mRNA level in each sample was calculated using ΔΔCT (i.e., ΔCT [treated sample] −ΔCT [untreated sample]) method. Each experiment was performed in triplicate.

Statistical analysis

SPSS software (version 21.0; IBM, Chicago, IL, USA) was used for all calculations. The distributions of all numerical variables, including *BMP-2*, *BMP-4*, *SPARC*, *COL1A1*, *OSGIN-1*, *MMP-3*, *IL-6*, and *HMOX1* mRNA levels, were skewed; thus, results were reported as medians and interquartile ranges. The Mann–Whitney U-test was used to compare numerical variables between groups. A $P < 0.05$ was considered statistically significant.

Results

Microarray data analyses

Only genes showing expression changes >2-fold after 1 mm TEGDMA treatment were taken into consideration. In total, 1282 and 1319 genes (up- or down-regulated) were differentially expressed compared with control group after 1- and 7-day incubationw periods, respectively. Of these, 276 genes were upregulated and 521 were downregulated in both time periods. Also, 481 and 518 genes exhibited statistically significant differential expression (up- or down-regulated) solely after 1- or 7-day incubation period, respectively. Transcripts with altered expression levels and biological, ontology-based analyses are reported in Supplementary Tables 1 and 2.

The largest groups of upregulated genes were involved in metabolic processes (GO: 0008152), cellular processes

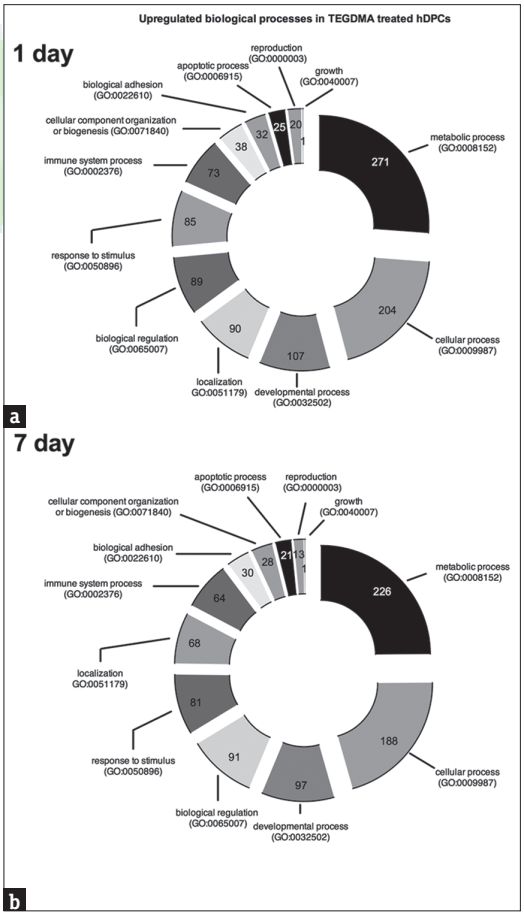

Figure 1: Diagram of the largest groups of upregulated biological processes in triethylene glycol dimethacrylate-treated human dental pulp cells after (a) 1- and (b) 7-day incubation period. The numbers designated in the pieces represent the number of genes those appear in any given category

Table 1: Primer sequence list in qRT-PCR

Target gene	Primer sequence	Annealing temperature (°C)
BMP-2	F:5'- CGGACTGCGGTCTCCTAA -3'	60
	R:5'- GGAAGCAGCAACGCTAGAAG -3'	
BMP-4	F:5'- ATGTGGGCTGGAATGACTGG -3'	
	R:5'- GCACAATGGCATGGTTGGTT -3'	
SPARC	F:5'- TGCAATGTGTTAGGGGATCTT -3'	
	R:5'- TGGTCTGCCTGCTAGAATGTT -3'	
COL1A1	F:5'- CCCAGCCACCTCAAGAGAAG -3'	
	R:5'- GTTCTCGATCTGCTGGCTCA -3'	
OSGIN1	F:5'- CTATGAGGGTTACCGCAGCC -3'	
	F:5'- AGACCCCAAACACCTTCTCG -3'	
MMP-3	F:5'- CAAAACATATTTCTTTGTAGAGGACAA -3'	
	R:5'- TTCAGCTATTTGCTTGGGAAA -3'	
IL-6	F:5'- CAGGAGCCCAGCTATGAACT-3'	
	R:5'- GAAGGCAGCAGGCAACAC-3'	
HMOX1	F:5'- CAGTCAGGCAGAGGGTGATAG-3'	
	R:5'- AGCTCCTGCAACTCCTCAAA-3'	
β-Actin	F:5'- ACTCTTCCAGCCTTCCTTCC -3'	
	R:5'- CGTACAGGTCTTTGCGGATG -3'	

BMP-2=Bone morphogenetic protein-2; *BMP-4*=Bone morphogenetic protein-4; *SPARC*=Secreted protein, acidic, cysteine-rich; *COL1A1*=Collagen type I alpha 1; *OSGIN1*=Oxidative stress-induced growth inhibitor 1; *MMP-3*=Matrix metallopeptidase-3; *IL-6*=Interleukin-6; *HMOX1*=Heme oxygenase-1

Table 2: Genes those showed up- and down-regulation of more than 10-fold changes after 1 mm triethylene glycol dimethacrylate treatment

Incubation period	Upregulated	Downregulated
1 day	AGPAT9, ANGPTL4, AREG, CLGN, DNER, GNLY, IL13RA2, KCNN4, MMP10, MMP12, PTGS1, SERPINB2, STC1, TFPI2, THBD	ASPN, CCL8, CNN1, COL11A1, COL14A1, COL15A1, COL1A1, COL3A1, CXCL12, CXCL6, DSP, EFEMP1, ELOVL2, FMOD, FNDC1, IGF2, IGFBP3, IGFBP5, NREP, PAPPA, PDGFD, PLXNC1, PMEPA1, POSTN, RBMS3, RHOBTB1, RNF150, SORBS2, SULF2, VCAM1, VCAN, WFDC1
7 days	CCDC68, DKK1, DNER, EREG, IL13RA2, KCNN4, KRTAP1-5, NPTX1, SERPINB2, TFPI2, THBD	ADAMTS5, ASNS, ASPN, BCAT1, CALD1, CCL8, CCL11, CH25H, CNN1, COL11A1, COL14A1, COL15A1, COL1A1, CSTA, CXCL12, ECM2, EFEMP1, EGFL6, FMOD, FNDC1, HEPH, HMCN1, IGF2, IGFBP3, IGFBP5, MAF, MFAP4, OLFML3, PAPPA, PLXNC1, PMEPA1, POSTN, PTGDS, RHOBTB1, SAMD5, SCD, SORBS2, SULF2, TAGLN, TENM2, VCAN, WFDC1

The underlined genes represent the highest fold changes

(GO: 0009987), developmental processes (GO: 0032502), localization (GO: 0051179), biological regulation (GO: 0065007), responses to stimuli (GO: 0050896), immune system processes (GO: 0002376), cellular component organization or biogenesis (GO: 0071840), biological adhesion (GO: 0022610), apoptotic processes (GO: 0006915), reproduction (GO: 0000003), and growth (GO: 0040007) [Figure 1]. The largest groups of downregulated genes were involved in metabolic processes (GO: 0008152), cellular processes (GO: 0009987), developmental processes (GO: 0032502), biological regulation (GO: 0065007), multicellular organismal processes (GO: 0032501), immune system processes (GO: 0002376), localization (GO: 0051179), responses to stimuli (GO: 0050896), biological adhesion (GO: 0022610), cellular component organization or biogenesis (GO: 0071840), apoptotic processes (GO: 0006915), reproduction (GO: 0000003), locomotion (GO: 0040011), and growth (GO: 0040007) [Figure 2].

The genes that showed expression changes >10-fold are listed in Table 2. The *THBD* gene exhibited the highest expression level, with 88.54- and 57.65-fold changes after 1- and 7-day incubation periods, respectively. The *COL1A1* and *FDNC1* genes showed the most dramatic downregulation, with −57.48- and −128.02-fold changes, respectively.

qRT-PCR validation

The microarray data were validated using qRT-PCR on the following genes: *BMP-2, BMP-4*, *SPARC*, *COL1A1*,

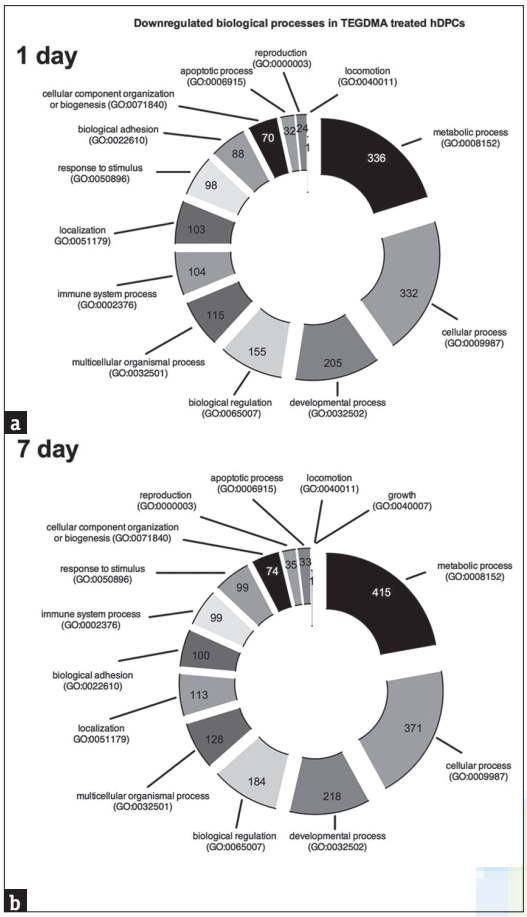

Figure 2: Diagram of the largest groups of downregulated biological processes in triethylene glycol dimethacrylate-treated human dental pulp cells after (a) 1- and (b) 7-day incubation period. The numbers designated in the pieces represent the number of genes those appear in any given category

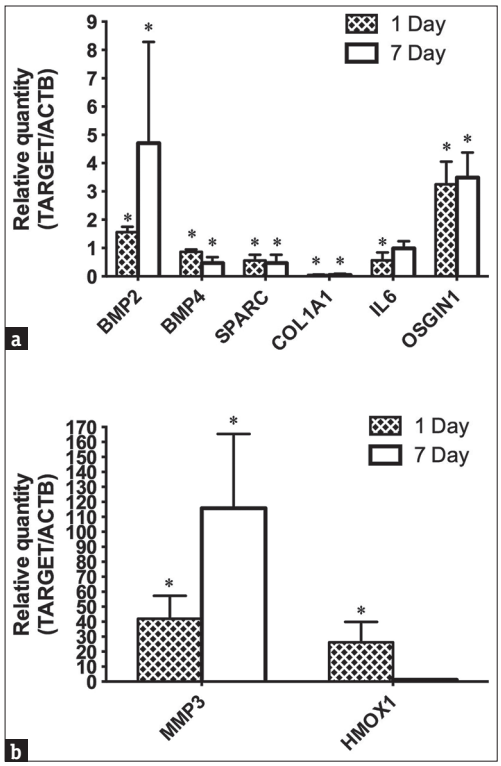

Figure 3: Verification of the microarray data using qRT-PCR on the following genes: (a) Bone morphogenetic protein-2, bone morphogenetic protein-4, secreted protein, acidic, cysteine-rich, collagen type I alpha 1, interleukin-6, oxidative stress-induced growth inhibitor 1, (b) matrix metalloproteinase 3, and heme oxygenase-1. Statistically significant differences are indicated by asterisks ($P < 0.05$)

OSGIN-1, *MMP-3*, *IL-6*, and *HMOX1*. These eight genes are related to mineralization, bone formation, ECM formation, DNA damage, oxidative stress, apoptosis, and inflammation. qRT-PCR results are shown in Figure 3. The qRT-PCR results confirmed the changes in expression revealed by the microarray analysis. hDPCs treated with 1 mm TEGDMA showed increased expression levels of *BMP-2*, *OSGIN-1, MMP-3*, and *HMOX1*, and decreased expression of *BMP-4*, *SPARC*, *COL1A1*, and *IL-6* (all $P < 0.05$) compared with control group.

Discussion

Resin monomers are used quite widely in dental practice. However, monomers cause many adverse biological effects in exposed cells and disturbance in many regulatory cellular mechanisms in cells interacting with some of these monomers. Previous studies have used high-throughput technologies such as DNA microarray and RNA-seq to investigate the biological effects of TEGDMA on skin fibroblasts and hDPCs, respectively.[9,11] These studies revealed that TEGDMA leads to considerable gene expression changes over time and affects many different signaling pathways. However, the effects of TEGDMA interacting with hDPCs over a relatively long time period are not understood. Knowledge of the cellular mechanisms associated with the adverse effects of TEGDMA will provide a better understanding to improve materials being used and may lead to innovative therapeutic strategies. In this study, we sought to determine the effects of TEGDMA on hDPCs after a 7-day exposure period. The results of this study confirmed a highly variable gene expression profile of hDPCs after exposure to TEGDMA and the capacity of TEGDMA to induce DNA damage, oxidative stress, apoptosis, inflammation, and negative regulation of dentin mineralization.

Metabolic, cellular, and developmental processes were the most affected biological functional annotations in both up- and down-regulated transcripts. However, cell-cell signaling, cell-cell adhesion, cell cycle, induction of apoptosis, cell death, macrophage activation, ion transport, and responses to stress were the most affected subgroups of biological processes [Appendix Tables 1 and 2]. The competence of cells to sense and respond to their microenvironment is the basis

of development, tissue repair, and immunity, as well as normal tissue homeostasis. These results reflect that the genes showing the greatest changes in hDPCs exposed to TEGDMA were associated primarily with basic cellular activities, such as inflammation and wound healing, and that TEGDMA causes changes in the coordination of cell actions. TEGDMA also caused some unusual systemic biological effects associated with fertilization and gamete generation. hDPCs are localized in an environment that is surrounded by hard dentin tissue, and nutritional support for hDPCs comes only through vessels in root canals. Thus, investigation of the release of unpolymerized dental resin monomers into the systemic circulation and possible effects on fertility is an important research topic.[14,15]

In addition, the results of the present study revealed important findings regarding the influence of TEGDMA on the mineralization of pulp cells. The genes most associated with pulp mineralization in this study were *BMP-2*, *BMP-4*, *SPARC*, and *COL1A1*. These genes encode ECM proteins and are used as markers of odontoblastic differentiation.[16-18] TEGDMA exhibited both positive and negative regulation on the expression of mineralization-related genes. While hDPCs showed an increase in *BMP-2* expression after exposure to TEGDMA, *BMP-4*, *SPARC*, and *COL1A1* were decreased in a time-dependent manner. The results of the present study are consistent with a recent study that concluded that the dose of TEGDMA applied, and the influence of TEGDMA on the different intracellular signaling pathways might affect the mineralization of pulp cells in different ways.[11] In addition, Galler *et al*. showed that TEGDMA caused dose- and time-dependent decreases in the expression of genes associated with pulp mineralization, including collagen I, alkaline phosphatase, bone sialoprotein, osteocalcin, Runx2, and dentin sialophosphoprotein.[3] Moreover, our results provide insights into other mineralization-related genes and have expanded the effects of TEGDMA on dentin mineralization.

Wound healing is a complex process in which hemostasis, inflammation, angiogenesis, ECM formation, remodeling by cell death, and apoptosis constitute some of the important stages in this process.[19] The results of the present study provide significant data regarding the effects of TEGDMA on tissue repair. hDPCs exposed to TEGDMA showed up- and down-regulation in genes mostly associated with responses to oxidative stress and inflammation. In addition, angiogenesis-, blood coagulation-, proliferation-, and differentiation-related genes were also identified, which changed significantly over time [Appendix Tables 1 and 2]. *OSGIN-1*, oxidative stress-induced growth inhibitor 1, encodes an oxidative stress response protein and regulates apoptosis.[20] It also appears to be a key regulator of both inflammatory and anti-inflammatory molecules. *HMOX1* plays a key role in the metabolism of heme and acts as a protective mechanism in the presence of oxidative stress.[21,22] In the present study, TEGDMA-exposed hDPCs exhibited upregulated expression of the *OSGIN-1* gene after 1- and 7-day exposure periods compared with control group. However, TEGDMA caused a greater fold change only after 1-day incubation whereas a significant expression change after 7-day incubation period was not detected. This might reflect the massive expression of *HMOX1* after the early exposure stage of hDPCs as an indicator of the initial protective effect of *HMOX1* against TEGDMA-induced reactive oxygen species, and other genes, such as *OSGIN-1*, continue to function as a part of the oxidative stress-induced biological pathways. Previous studies have already shown initial *HMOX1* expression in TEGDMA-treated hDPCs.[11] However, *OSGIN-1* and associated signaling pathways seem to be an attractive research area to examine the TEGDMA-hDPCs interaction in terms of responses to oxidative stress.

Matrix metallopeptidase (MMP) are calcium- and zinc-dependent endopeptidases that play roles in the remodeling and degradation of ECM.[23] However, the role of MMPs in wound healing is unclear. While Hiyama *et al*. reported that *MMP-3* promotes and accelerates wound healing, Beidler *et al*. and Liu *et al*. reported that elevated MMP levels are associated with nonhealing.[24-26] *MMP-3* was upregulated after 1- and 7-day exposure times in the present study. This suggests that *MMP-3* may be involved in the wound healing process of pulp tissue treated with TEGDMA via reorganization of the ECM. However, further studies are needed to establish whether *MMP-3* increases or reduces wound healing in TEGDMA-treated hDPCs.

IL-6 acts as a pro- and anti-inflammatory cytokine, and the release of this cytokine is important in the initiation of inflammatory processes after exposure to harmful foreign pathogens, such as viruses, bacteria, and chemicals.[13] Various studies have been carried out on different cell lines to show the effects of resin monomers on *IL-6 sec*retion, and different results were obtained regarding the responses of the cells. A TEGDMA-treated three-dimensional human tissue model constructed from TR146 cells revealed an increase in the secretion of *IL-6*.[27] It has also been reported that costimulation of macrophages with lipopolysaccharides and TEGDMA resulted in a dose-dependent decrease in the secretion of *IL-6*.[13] However, no significant change was detected

in *IL*-6 production after the macrophages were treated with increasing concentrations of TEGDMA alone. In the present study, *IL-6* expression in TEGDMA-exposed hDPCs was inhibited after 1-day incubation period. However, we did not detect a significant expression change after 7-day incubation period. Although there are some contradictions, current and previous results described here reveal that TEGDMA has an important effect on inflammatory processes in terms of its inhibition and/or stimulation. Experimental conditions and differences in the cell lines used may be a cause of the differences. However, the results presented herein suggest that TEGDMA inhibits the innate immune system in hDPCs by inhibiting the production of cytokines, including *IL*-6. Disturbances of the innate immune system in the presence of TEGDMA may prevent hDPCs from generating a proper immune response and make the host vulnerable to pathogens.

Taken together, these findings revealed that various biological pathways contribute to the adverse effects of TEGDMA on hDPCs. Physical properties, such as low molecular weight and relatively high hydrophilicity, are the important factors for the penetration of TEGDMA to all biological compartments, and this may be the cause of different chemical-biological interactions with intracellular processes.[28] The present study revealed that the vast majority of the differentially regulated transcripts play a role in DNA damage, oxidative stress, apoptosis, and negative regulation of dentin mineralization. Besides, TEGDMA revealed important changes in the inflammation and wound healing processes. Biocompatibility is defined as the absence of inflammatory, irritating, toxic, or genotoxic effects in biological systems and the aforementioned data revealed that TEGDMA does not have most of these biocompatibility features and cause multiple adverse effects on interacting cells. Consequently, it should be the aim of future studies to show the effects of TEGDMA in detail about interactions with intracellular processes and to develop more biocompatible monomers.

The small number of samples analyzed is a limitation of this study. However, the data provide new information about the gene expression profiles of hDPCs in response to TEGDMA treatment.

Conclusions

While the detailed mechanism of toxicity is not completely understood, the present study revealed that TEGDMA can change the many functions of hDPCs through large changes in gene expression levels and complex interactions with different signaling pathways.

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Conflicts of interest

There are no conflicts of interest.

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Appendix Table 1: Up-regulated transcripts and biological, ontology-based analyses in triethylene glycol dimethacrylate-treated dental pulp cells

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Apoptotic process (GO:0006915)	25	21	4.4	4.4	Induction of apoptosis (GO:0006917)	CAPN2, FOSL1, L1CAM, LIF, NOVA1, RIPK3, SMOX, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21	CAPN2, FOSL1, IGF2BP3, LIF, LIMK1, NOVA1, RIPK3, TNFRSF1B, TNFRSF21	Induction of apoptosis (GO:0006917)	11	9
					Negative regulation of apoptotic process (GO:0043066)	DNAJB14, DNAJB9, LIF, MYBL1, SOCS3, TMBIM1, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21	BIRC3, CD163L1, HDAC9, LIF, LOXL4, MYBL1, TNFRSF1B, TNFRSF21	Negative regulation of apoptotic process (GO:0043066)	10	8
Biological adhesion (GO:0022610)	32	30	5.6	6.3	Cell adhesion (GO:0007155)	ANGPTL4, ATL1, CD151, CD46, CD55, CD9, CIT, CLMP, COL10A1, CTSL1, CUZD1, DCBLD2, DNER, F8, ITGA10, ITGA2, ITGA3, ITGA5, ITGA6, L1CAM, LAMA5, LAMC2, MTSS1, MYPN, NTN4, NTNG1, PGS1, SGIP1, SMAP2, TSPAN12, TSPAN13, VNN1	ANGPTL4, ATL1, CD163L1, CD9, CIT, CLMP, COL10A1, COL13A1, COL4A5, CTSL1, DCBLD2, DNER, ITGA10, ITGA2, ITGA3, ITGA6, LAMA3, LAMA5, LAMC2, LOXL4, MTSS1, MYPN, NTN4, PGS1, RAP1GAP2, SGIP1, SMAP2, TSPAN12, TSPAN13, VNN1	Cell-cell adhesion (GO:0016337)	20	18
								Cell-matrix adhesion (GO:0007160)	6	6
Biological regulation (GO:0065007)	89	91	15.6	19.0	Homeostatic process (GO:0042592)	ATP2A3, EDNRB, GPR39, HK2, SOCS3, STC1	ATP2A3, ATP8B1, CALB2, COL13A1, COL4A5, EDNRB, GPR39, HK1, HKDC1, STC1	Cellular calcium ion homeostasis (GO:0006874)	2	4
								Cellular glucose homeostasis (GO:0001678)	3	2
								Regulation of liquid surface tension (GO:0050828)		2
					Regulation of biological process (GO:0050789)	ADRB2, CBX7, CLU, CNOT6L, CREM, DNAJB14, DNAJB9, DNER, DUSP10, DUSP6, EDNRB, EIF3G, ETS2, ETV1, FOSL1, HMGA1, KLF4, KLF8, LIF, MAFF, MYBL1, NCOA3, NR0B1, NR4A2, NRIP3, PDK4, PHF19, PITX1, PLAG1, PPARG, PRDM8, PSPC1, RFX8, RGS20, SALL1, SERPINB2, SERPIND1, SERPINE1, SERPING1, SERPINI1, SFRP1, SFRP2, SOCS3, STC1, TCF7, TFAP2A, TFAP2C, TMBIM1, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21, TOX2,	ADRB2, ANKRD22, BDKRB1, BIRC3, CD163L1, CLU, DNER, DUSP6, EDNRB, EFTUD1, EIF4A2, ETS2, ETV1, FOSL1, FZD8, HDAC9, HMGA1, HMGA2, KCNMA1, LIF, LOXL4, MAFF, MEOX1, MYBL1, MYC, NCOA3, NPAS3, NR0B1, NR5A2, PAX3, PDE12, PDK4, PITX1, PLAG1, POU2F2, PPARG, RFX8, RGS17, RGS20, RGS7, SALL1, SERPINB2, SERPINB8, SERPINE1, SERPINE2,	Negative regulation of apoptotic process (GO:0043066)	10	8
								Regulation of cell cycle (GO:0051726)		1
								Regulation of cellular amino acid metabolic process (GO:0006521)	1	1
								Regulation of nucleobase-containing compound metabolic process (GO:0019219)	33	32
								Regulation of phosphate metabolic process (GO:0019220)	3	4
								Regulation of translation (GO:0006417)	2	3

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Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
						TWIST2, WNT16, WNT5B, ZNF425, ZNF451, ZNF557	SERPINI1, SFRP1, SFRP2, SMURF2, SOX15, STC1, TCF7, TFAP2A, TNFRSF1B, TNFRSF21, TRIM36, TWIST2, WNT16, WNT5B, ZNF557	Regulation of vasoconstriction (GO:0019229)	2	3
					Regulation of molecular function (GO:0065009)	ARFIP2, ATL1, BCR, CCNB1, CCND1, CCND3, CDK2AP2, CST1, CST3, CUZD1, DCBLD2, DUSP10, EHD1, F8, HPCAL1, LRRC8C, MLPH, NCALD, PLCD4, PPP1R1C, PREX1, RGS20, RIN1, SEC23B, SERPINB2, SERPIND1, SERPINE1, SERPING1, SERPINI1, SMAP2, SOCS3, TBC1D15, TBC1D8, TFPI2, TIMP4	ARHGAP20, ATL1, BCR, BIRC3, CCND1, CCNE2, CYFIP2, DCBLD2, EHD1, GMFG, HPCAL1, LRRC2, MLPH, PREX1, RAP1GAP2, RASGRP3, RGS17, RGS20, RGS7, RIN1, SEC23B, SERPINB2, SERPINB8, SERPINE1, SERPINE2, SERPINI1, SMAP2, TBC1D8, TFPI, TFPI2, TRIOBP, ZFR	Regulation of catalytic activity (GO:0050790)	35	32
Cellular component organization or biogenesis (GO:0071840)	38	28	6.7	5.8	Cellular component biogenesis (GO:0044085)	HYOU1, YME1L1, HSPA5	RPS28	Protein complex biogenesis (GO:0070271)	3	1
					Cellular component organization (GO:0016043)	ARFIP2, CAPG, CBX7, CIT, COL10A1, CORO2B, FRMD4B, GLDN, HIP1R, HIST1H1C, HIST1H2AB, HIST1H2AG, HIST1H2BC, HIST1H2BJ, HIST1H2BK, HIST2H2AA3, INA, KIF18A, KIF21A, KIF3C, KIFC2, MLPH, NPY, RIPK3, SMOX, SMTN, SVIL, TBC1D15, TBC1D8, TOX2, TUBG2, WHSC1, YME1L1	ABLIM3, ANK1, CIT, COL10A1, COL13A1, COL4A5, CORO2B, FRMD4B, FZD8, GLDN, HCLS1, HDAC9, HIST1H1C, HIST1H2AB, HIST1H2BD, INA, KRT34, LIMK1, MBP, MLPH, NPY, RIPK3, SVIL, TBC1D8, TRIOBP, TUBA4A	Cellular component morphogenesis (GO:0032989)	22	20
								Organelle organization (GO:0006996)	14	6

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Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Cellular process (GO:0009987)	204	188	35.7	39.2	Cell cycle (GO:0007049)	AURKA, CCNB1, CCND1, CCND3, CDC20, CDK2AP2, CDKN3, CELF2, CIT, EFCAB2, EMP1, EMP3, EPGN, EREG, ESPL1, ETS2, ETV1, FGF13, FOSL1, HMGA1, HS2ST1, KIF18A, KIF20A, KIF21A, KIF3C, KIFC2, L1CAM, MAD2L1, MTSS1, MYBL1, NOV, PARD6B, PGF, POLM, PRKAA2, RIPK3, SDAD1, TUBG2, VEGFA, VEGFC, WISP2	CCND1, CCNE2, CDC25A, CELF2, CIT, EMP1, EPGN, EREG, ETS2, ETV1, FASTKD2, FGF13, FOSL1, HDAC9, HMGA1, HMGA2, HS2ST1, LIMK1, MCM3, MCM4, MPHOSPH6, MTSS1, MYBL1, MYC, NOV, PGF, RASGRP3, RIPK3, SDAD1, SGK1, TRIM36, TUBA4A, VEGFC, WISP2, ZFR	Meiosis (GO:0007126)	7	1
								Mitosis (GO:0007067)	15	8
								Regulation of cell cycle (GO:0051726)		1
					Cell communication (GO:0007154)	ADRB2, ANGPTL4, ATL1, BCR, BMP2, CACNA1A, CAMK2G, CAPN2, CD151, CD46, CD55, CD9, CD97, CDK2AP2, CIT, CNIH3, CRABP2, CREM, CUZD1, CXCL11, CXCL5, DCBLD2, DEPDC1, DNER, DUSP10, DUSP6, EDNRB, EFCAB2, EHD1, EPGN, EREG, ETS2, ETV1, F8, FGF13, GABBR2, GLDN, GPCPD1, GPR125, GPR39, GPR56, HM13, HPCAL1, IL13RA2, IL24, IRAK2, ITPR3, L1CAM, LAMA5, LAMC2, LIF, LRRC8C, LYPLAL1, MEGF6, NCALD, NCOA3, NOV, NOVA1, NPY, NR4A2, NTN4, NTNG1, PAQR5, PARD6B, PDK4, PGF, PGS1, PLCD4, PPAPDC1A, PPARG, PPP1R1C, PRKAA2, PROCR, PTCH1, RAC2, RHOB, RHOU, RIPK3, SCN9A, SEC23B, SEMA3A, SEMA4F, SEMA6D, SFRP1, SFRP2, SGIP1, SH2B3, SLC1A1, SLC22A15, SLC22A23, SLC22A4, SLC6A15, SMAP2, SOCS3, SPRY2, SPRY4, SRI, STAMBPL1, STC1, STXBP1,	ABL2, ADRB2, ANGPTL4, ANKRD22, ARHGAP20, ATL1, BCR, BDKRB1, BMP2, CALB2, CAMK2G, CAPN2, CCRL1, CD163L1, CD9, CIT, CNIH3, COL13A1, COL4A5, CSF2, CXCL11, CXCL5, CYFIP2, DCBLD2, DNER, DTX4, DUSP6, EDNRB, EHD1, EPGN, EREG, ETS2, ETV1, F3, FGF13, FGF2, FZD8, GABBR2, GLDN, GPR39, GPR56, HPCAL1, IGF2BP3, IL12A, IL13RA2, IRAK2, ITPR3, LAMA3, LAMA5, LAMC2, LIF, LIMK1, LOXL4, LRRC2, LYPLAL1, MEGF6, NCOA3, NOV, NOVA1, NPY, NRG1, NTN4, PAQR5, PDK4, PGF, PGS1, PPAPDC1A, PPARG, PROCR, PTCHD4, RASGRP3, RIPK3, SCN9A, SEC23B, SEMA4F, SEMA6D, SFRP1, SFRP2, SGIP1, SGK1, SH2B3, SH2D5, SLC1A1, SLC1A2, SLC22A23, SLC22A4,	Cell-cell signaling (GO:0007267)	33	29

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Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
						SYT11, TACR1, TCF7, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21, TOX2, TSPAN12, TSPAN13, VEGFA, VEGFC, VNN1, WISP2, WNT16, WNT5B, ZFAND5	SLC6A15, SLC6A6, SMAP2, SMURF2, SPRY2, STAMBPL1, STC1, TACR1, TC2N, TCF7, TNFRSF1B, TNFRSF21, TRIOBP, TSPAN12, TSPAN13, VEGFC, VNN1, WISP2, WNT16, WNT5B			
					Cellular component movement (GO:0006928)	ARFIP2, ADRB2, CIT, DNER, EFCAB2, EGFL8, FMNL2, ITPR3, LPXN, MTSS1, NOV, NPY, PXN, SMTN, TUBG2, WISP2	ABLIM3, ADRB2, CIT, DNER, EGFL8, FHOD1, ITPR3, LPXN, MTSS1, NOV, NPY, PXN, SH2D5, TUBA4A, WISP2	Cellular component movement (GO:0006928)	16	15
					Chromosome segregation (GO:0007059)	HMGA1, KIF18A, KIF20A, KIF21A, KIF3C, KIFC2, MAD2L1, TUBG2	HMGA1, HMGA2, TUBA4A	Chromosome segregation (GO:0007059)	8	3
					Cytokinesis (GO:0000910)	AURKA, KIF18A, KIF20A, KIF21A, KIF3C, KIFC2		Cytokinesis (GO:0000910)	6	
Developmental process (GO:0032502)	107	97	18.7	20.3	Anatomical structure morphogenesis (GO:0009653)	ARFIP2, CAPG, CIT, COL10A1, DUSP4, DUSP5, DUSP6, FRMD4B, GLDN, HIP1R, INA, KIF18A, KIF20A, KIF21A, KIF3C, KIFC2, MBP, MLPH, MYPN, NPY, RIPK3, SMTN, SVIL, TBC1D15, TBC1D8, TUBG2	ABLIM3, ANK1, CIT, COL10A1, COL13A1, COL4A5, DUSP4, DUSP5, DUSP6, FRMD4B, FZD8, GLDN, HCLS1, INA, KRT34, LIMK1, MBP, MLPH, MYPN, NPY, RIPK3, SVIL, TBC1D8, TRIOBP, TUBA4A	Cellular component morphogenesis (GO:0032989)	22	20
					Cell differentiation (GO:0030154)	DUSP6, TCF7, WNT16, WNT5B	DUSP6, FZD8, TCF7, WNT16, WNT5B	Cell differentiation (GO:0030154)	4	5
					Death (GO:0016265)	ADAM15, ADRB2, CAPN2, CBX7, DNAJB14, DNAJB9, DUSP6, FOSL1, HGF, HIP1R, L1CAM, LIF, MYBL1, NOVA1, PLAG1, RIPK3, SMOX, SOCS3, TMBIM1, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21, UBE2D1, VAT1L	ADRB2, ANKRD22, BIRC3, CAPN2, CD163L1, DUSP6, FOSL1, HDAC9, HGF, IGF2BP3, LIF, LIMK1, LOXL4, MYBL1, NOVA1, PLAG1, RIPK3, TNFRSF1B, TNFRSF21, VAT1L, ZFR	Cell death (GO:0008219)	25	21

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Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Ectoderm development (GO:0007398)	BMP2, CELF2, CRABP2, CREM, CUZD1, DCBLD2, DNER, EDNRB, EMP1, F8, GLDN, L1CAM, LAMA5, MAML3, MTSS1, NR4A2, NTN4, PITX1, SEMA3A, SEMA4F, SEMA6D, SGIP1, TFAP2A, TFAP2C, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21	ABLIM3, BMP2, CELF2, COL13A1, COL4A5, DCBLD2, DNER, EDNRB, EMP1, GLDN, GMFG, LAMA3, LAMA5, MTSS1, NPAS3, NRG1, NTN4, PAX3, PITX1, SEMA4F, SEMA6D, SGIP1, SH2D5, TFAP2A, TNFRSF1B, TNFRSF21	Ectoderm development (GO:0007398)	28	26
					Embryo development (GO:0009790)	CIT, DUSP4, DUSP5, DUSP6	CIT, CPEB2, DUSP4, DUSP5, DUSP6, LIMK1	Embryo development (GO:0009790)	4	6
					Endoderm development (GO:0007492)	DUSP4, DUSP5, DUSP6	DUSP4, DUSP5, DUSP6	Endoderm development (GO:0007492)	3	3
					Mesoderm development (GO:0007498)	ADAM15, BMP2, CD97, COL10A1, CUZD1, DCBLD2, ETS2, ETV1, F8, FGF13, GPR125, GPR56, KLF4, KLF8, L1CAM, LPXN, MYPN, NOV, PBX1, PGS1, PITX1, PRKAA2, PTHLH, PXN, SEMA3A, SEMA4F, SEMA6D, SOCS3, SPRY2, SPRY4, SPRY4, TNFRSF1B, TWIST2, WISP2	BMP2, CDH6, COL10A1, COL13A1, COL4A5, DCBLD2, ETS2, ETV1, FGF13, GPR56, LPXN, MEOX1, MYPN, NOV, PAX3, PBX1, PCDH9, PGS1, PITX1, PTHLH, PXN, SEMA4F, SEMA6D, SH2D5, SPRY2, SPRYD4, TNFRSF1B, TWIST2, WISP2	Mesoderm development (GO:0007498)	34	29
					Pattern specification process (GO:0007389)	DUSP6, KLF8, PITX1	DUSP6, PAX3, PITX1, ZFR	Anterior/posterior axis specification (GO:0009948)	1	1
								Segment specification (GO:0007379)	1	2
					Sex determination (GO:0007530)	NR0B1	NR0B1	Sex determination (GO:0007530)	1	1

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Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					System development (GO:0048731)	ADAM15, ANGPTL4, BMP2, CAMK2G, CD97, CELF2, COL10A1, CREM, CUZD1, CXCL11, CXCL5, DCBLD2, DUSP6, EDNRB, ETS2, ETV1, F8, FGF13, GLDN, GPR125, GPR56, IL13RA2, KLF4, KLF8, L1CAM, LAMA5, LPXN, MAML3, MTSS1, MYPN, NOV, NTN4, NTNG1, PBX1, PGF, PGS1, PITX1, PRKAA2, PTHLH, PXN, SEMA3A, SEMA4F, SEMA6D, SFRP1, SFRP2, SGIP1, SOCS3, SPRY4, TCF7, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21, TWIST2, VEGFA, VEGFC, WISP2, WNT16, WNT5B	ABLIM3, ANGPTL4, BMP2, CAMK2G, CDH6, CELF2, COL10A1, CXCL11, CXCL5, DCBLD2, DUSP6, EDNRB, ETS2, ETV1, FGF13, FZD8, GLDN, GMFG, GPR56, IL13RA2, LAMA3, LAMA5, LPXN, MEOX1, MTSS1, MYPN, NGF, NOV, NPAS3, NRG1, NTN4, PAX3, PBX1, PCDH9, PGF, PGS1, PITX1, PTHLH, PXN, SEMA4F, SEMA6D, SFRP1, SFRP2, SGIP1, SH2D5, SPRYD4, TCF7, TNFRSF1B, TNFRSF21, TWIST2, VEGFC, WISP2, WNT16, WNT5B	Angiogenesis (GO:0001525)	18	12
								Heart development (GO:0007507)	13	9
								Hemopoiesis (GO:0030097)	5	4
								Muscle organ development (GO:0007517)	4	7
								Nervous system development (GO:0007399)	30	32
								Skeletal system development (GO:0001501)	9	9
Growth (GO:0040007)	1	1	0.2	0.2	Growth (GO:0040007)	DUSP6	DUSP6	Growth (GO:0040007)	1	1
Immune system process (GO:0002376)	73	64	12.8	13.4	Antigen processing and presentation (GO:0019882)	CTSS, MICA, RAET1G		Antigen processing and presentation of peptide or polysaccharide antigen via MHC class II (GO:0002504)	1	
					Immune response (GO:0006955)	ADRB2, ATL1, CCL26, CCL5, CD55, CD97, CLEC2B, COL10A1, CXCL11, CXCL5, ETS2, ETV1, GPR125, GPR56, IL13RA2, IL24, KLF4, KLF8, MASP1, MICA, NPTX1, POLM, RAET1G, SH2B3, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21	ADRB2, ATL1, CCL5, CCRL1, CLEC2B, COL10A1, CSF2, CXCL11, CXCL5, ETS2, ETV1, F3, GPR56, IL12A, IL13RA2, NPTX1, SH2B3, TNFRSF1B, TNFRSF21, ZFR	B cell-mediated immunity (GO:0019724)	14	7
								Complement activation (GO:0006956)	3	1
								Natural killer cell activation (GO:0030101)	1	3
								Response to interferon-gamma (GO:0034341)	1	3
					Macrophage activation (GO:0042116)	ADRB2, ATL1, CD97, COLEC12, CXCL11, CXCL5, ETS2, ETV1, IL24, SCARA5, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21	ADRB2, ATL1, CD163L1, COL4A5, COLEC12, CXCL11, CXCL5, ETS2, ETV1, F3, IL12A, LOXL4, SCARA5, TNFRSF1B, TNFRSF21	Macrophage activation (GO:0042116)	14	15

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Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Localization (GO:0051179)	90	68	15.8	14.2	Protein localization (GO:0008104)	PARD6B, STX1A	STX1A	Asymmetric protein localization (GO:0008105)	1	1
					RNA localization (GO:0006403)	CFEB1	CPEB2, RPS28, ZFR	RNA localization (GO:0006403)	1	3
					Transport (GO:0006810)	ABCA3, ABCA6, ABCG2, ACSL4, ADRB2, AKR1B1, AKR1C1, ALG10, AP2M1, ATP2A3, ATP6V0B, ATP6V0C, ATP6V0E2, ATP6V1G2-DDX39B, BET1, CACNA1A, CD46, CD55, CD68, CD97, CLCA2, CLGN, CNIH3, COLEC12, CRABP2, CUZD1, DCBLD2, EHD1, ERO1LB, F8, FXYD5, GLDN, GPR125, GPR56, ITPR3, KCNN4, KIF18A, KIF20A, KIF21A, KIF3C, KIFC2, MFSD8, MLPH, NOVA1, NRIP3, PITPNC1, PKD1P1, PPIF, PREB, PTCH1, RAC2, RHOB, RHOU, RIN1, SCARA5, SCN9A, SEC23B, SLC12A7, SLC16A14, SLC16A4, SLC16A6, SLC1A1, SLC20A1, SLC22A15, SLC22A23, SLC22A4, SLC31A2, SLC35B1, SLC35E4, SLC35G2, SLC37A2, SLC47A1, SLC6A15, SLCO4A1, SNCA, SOCS3, STX1A, STXBP1, SYT11, SYT7, TBC1D15, TBC1D8, TMED5, TRPV2, TUBG2, UCP2, XPO1, YME1L1	ABCA6, ABCA8, ABCD3, ABCG2, ACSL4, ADRB2, AKR1B1, AKR1B10, AKR1B15, AKR1C1, ANKRD22, ATP2A3, ATP8B1, CD163L1, CD68, CLCA2, CLGN, CNIH3, COL13A1, COL4A5, COLEC12, DCBLD2, DNAJC6, EHD1, GLDN, GPR56, IGF2BP3, ITPR3, KCNMA1, KCNN4, LOXL4, MCOLN3, MLPH, NOVA1, OSBPL3, PPIF, PTCHD4, RIN1, RPS28, SCAMP3, SCARA5, SCFD2, SCN9A, SEC23B, SLC12A7, SLC16A2, SLC16A6, SLC17A5, SLC1A1, SLC1A2, SLC20A1, SLC22A23, SLC22A4, SLC47A1, SLC6A15, SLC6A6, SLC7A14, SLCO2B1, SLCO4A1, SNCA, STX1A, TBC1D8, TC2N, TPCN1, TRPV2, TUBA4A, ZFR	Amino acid transport (GO:0006865)	3	5
								carbohydrate transport (GO:0008643)	6	3
								Extracellular transport (GO:0006858)	5	7
								ion transport (GO:0006811)	26	22
								Lipid transport (GO:0006869)	13	9
								Lysosomal transport (GO:0007041)	3	3
								mitochondrial transport (GO:0006839)	1	
								Nuclear transport (GO:0051169)	3	4
								nucleobase-containing compound transport (GO:0015931)	3	2
Metabolic process (GO:0008152)	271	226	47.5	47.2	Biosynthetic process (GO:0009058)	PLAG1, TCF7	PLAG1, TCF7	Biosynthetic process (GO:0009058)	2	2
					Catabolic process (GO:0009056)	HACE1, HK2, GLA, NEDD4L, RGS20	GLA, HERC5, HK1, HKDC1, RGS17, RGS20, RGS7, SMURF2	Catabolic process (GO:0009056)	5	8

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Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Coenzyme metabolic process (GO:0006732)	ACADVL, AUH, DLST, MTHFSD		Acyl-CoA metabolic process (GO:0006637)	1	
					Generation of precursor metabolites and energy (GO:0006091)	ACADVL, ADCK2, COX7A2, CYP19A1, CYP26B1, ERO1LB, HK2, NDUFS2, SMOX, UGDH, XDH, ZFAND5	COX7A2, CYP26B1, HK1, HKDC1, MDH2, NDUFS2, TXNRD1, UGDH, XDH	Oxidative phosphorylation (GO:0006119)	3	2
								Respiratory electron transport chain (GO:0022904)	11	6
					Nitrogen compound metabolic process (GO:0006807)	ACADVL, GLA, GLUL, HMOX1, PLAG1, RGS20, SMOX, TCF7	GLA, PLAG1, RGS17, RGS20, RGS7, TCF7, TXNRD1	Porphyrin-containing compound metabolic process (GO:0006778)	2	
					Phosphate-containing compound metabolic process (GO:0006796)	ABCA3, ABCA6, ACYP1, DUSP10, DUSP4, DUSP5, DUSP6, GLDN, HK2, MGLL, NEK2, NUDT7, PBK, PLCD4, PPAPDC1A, RGS20, RIPK3, SLC20A1, SLC22A15, SLC22A23, SLC22A4, SLC37A2, STC1, UCP2	ABCA6, ABCA8, ACYP1, ANKRD22, CDC25A, DUSP4, DUSP5, DUSP6, GLDN, HK1, HKDC1, LIMK1, PLA2G15, PPAPDC1A, RGS17, RGS20, RGS7, RIPK3, SLC17A5, SLC20A1, SLC22A23, SLC22A4, STC1	Phospholipid metabolic process (GO:0006644)	5	5
								Regulation of phosphate metabolic process (GO:0019220)	3	4
					Primary metabolic process (GO:0044238)	ABCA3, ABCA6, ABCG2, ABHD14A-ACY1, ABHD6, ACADVL, ACSL4, ADRB2, AK2, AK4, AMDHD1, AMPD3, ANPEP, ANXA11, APOBEC3B, ATL1, ATP6V1G2-DDX39B, AUH, AURKA, BTBD11, CAMK2G, CAPN2, CBX7, CD46, CD55, CD68, CDC20, CDK2AP2, CDKN3, CDO1, CELF2, CHST2, CIT, CLGN, CLPTM1, CLU, CNOT6L, CPEB1, CPXM2, CRABP2, CREM, CST1, CST3, CSTF3, CTBS, CTSF, CTSL1, CTSS, CUZD1, CXXC1, CYP19A1, DCBLD2, DLST, DNAJA3, DNAJB14, DNAJB9, DNER, DPP4,	ABCA6, ABCA8, ABCD3, ABCG2, ABL2, ACSL4, ADRB2, ALDH3A1, AMDHD1, AMPD3, ANKRD22, ANPEP, ANXA11, ATL1, ATP8B1, B3GAT3, BTBD11, BTBD3, CAMK2G, CAMKK1, CAPN2, CD163L1, CD68, CDC25A, CDO1, CELF2, CHST2, CIT, CLGN, CLU, CPA4, CPEB2, CSTF3, CTBS, CTSL1, DCAF13, DCBLD2, DENND3, DNAJC6, DNER, DPP4, DTX4, DUSP4, DUSP5, DUSP6, EDEM2, EDNRB, EFTUD1, EIF4A2, ENPP2,	carbohydrate metabolic process (GO:0005975)	30	26
								Cellular amino acid metabolic process (GO:0006520)	15	12
								Lipid metabolic process (GO:0006629)	25	22
								Nucleobase-containing compound metabolic process (GO:0006139)	72	64
								protein metabolic process (GO:0019538)	92	79

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Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
						DUSP10, DUSP4, DUSP5, DUSP6, EDNRB, EIF3G, ENPP2, ENPP4, ENTPD1, ERO1LB, ETS2, ETV1, F8, FKBP1A, FOSL1, GALE, GALNT12, GALNT6, GBA, GGT1, GK, GLA, GLB1L, GLUL, GPR39, GPR89A, GPX3, HACE1, HAS3, HIPK2, HIST1H1C, HIST1H2AB, HIST1H2AG, HIST1H2BC, HIST1H2BD, HIST1H2BJ, HIST1H2BK, HIST2H2AA3, HK2, HMGA1, HS2ST1, HSD3B7, HSPA5, HSPB8, HYOU1, IRAK2, KLF4, KLF8, KYNU, L1CAM, LRRC8C, LYPLAL1, MAFF, MARS2, MASP1, MFSD8, MGLL, MMP10, MMP3, MYBL1, MYPN, NCOA3, NEDD4L, NEK2, NOVA1, NR0B1, NR4A2, NRIP3, NT5E, ODC1, PAMR1, PAQR5, PBK, PBX1, PDK4, PHF19, PIGF, PIGW, PITPNC1, PITX1, PLAG1, PLAT, PLAU, PLCD4, PNP, POLM, PPAPDC1A, PPARG, PPIF, PRDM8, PREB, PRKAA2, PSPC1, PTCH1, PTPN3, PYGB, QPCT, RFX8, RGS20, RIPK3, RNF157, RPP25, SALL1, SDF2L1, SELT, SERPINB2, SERPIND1, SERPINE1, SERPING1, SERPINI1, SGIP1, SLC1A1, SLC22A15, SLC22A23, SLC22A4, SLC35B1, SLC35E4, SLC37A2, SLC3A2, SLC6A15, SMOX, SPRY4, SRI, SRSF5, SYVN1, TCF7, TFAP2A, TFAP2C, TFPI2, TIMP4, TMX3, TOR4A, TOX2, TWIST2, UBE2D1, UCP2, UGDH, UGGT2, UPP1, USP36, VAT1L, WHSC1, XDH, XPO1, YME1L1, ZNF425, ZNF451, ZNF557	ENPP4, ERMP1, ETS2, ETV1, FDXACB1, FKBP1A, FOSL1, G6PD, GALE, GALNT12, GBA, GCNT3, GLA, GLB1L, GM2A, GPR39, HADH, HAS3, HCLS1, HDAC9, HERC5, HIPK2, HIST1H1C, HIST1H2AB, HIST1H2BD, HK1, HKDC1, HMGA1, HMGA2, HS2ST1, HSD3B7, HSPB8, IGF2BP3, IRAK2, KYNU, LIMK1, LOXL4, LRRC2, LYPLAL1, MAFF, MARS2, MCM3, MCM4, MDH2, MEOX1, MMP10, MMP3, MYBL1, MYC, MYPN, NCOA3, NOVA1, NPAS3, NPM1, NR0B1, NR5A2, NT5E, OSBPL3, PAMR1, PAQR5, PAX3, PBX1, PDE12, PDK4, PIGW, PITX1, PLA2G15, PLAG1, PLAT, PLAU, PNP, POU2F2, PPAPDC1A, PPARG, PPIF, PSMC2, PTCHD4, PTPN3, QPCT, RFX8, RGS17, RGS20, RGS7, RIPK3, RNF157, RPP25, SALL1, SERPINB2, SERPINB8, SERPINE1, SERPINE2, SERPINI1, SF3B3, SGIP1, SGK1, SLC17A5, SLC1A1, SLC1A2, SLC22A23, SLC22A4, SLC6A15, SLC6A6, SLC7A14, SMURF2, SOX15, SPRYD4, SQSTM1, STIP1, TCF7, TFAP2A, TFPI, TFPI2, TIPARP, TMX4, TOR4A, TRIM36, TWIST2, TXNRD1, TYSND1, UGDH, UGGT2, USP53, VAT1L, WHSC1, XDH, ZBTB21, ZFR, ZNF557	Tricarboxylic acid cycle (GO:0006099)		1

Contd...

Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Sulfur compound metabolic process (GO:0006790)	HS2ST1	HS2ST1	Sulfur compound metabolic process (GO:0006790)	1	1
					Vitamin metabolic process (GO:0006766)	AUH, GGH, VNN1	VNN1	Vitamin biosynthetic process (GO:0009110)	1	1
Multicellular organismal process (GO:0032501)	56	54	9.8	11.3	Single-multicellular organism process (GO:0044707)	ADAM15, ADRB2, CACNA1A, CD151, CD9, CD97, CELF2, CREM, CUZD1, DCBLD2, DUSP4, DUSP5, DUSP6, EDNRB, EHD1, F8, FOSL1, GABBR2, GPR125, GPR39, GPR56, HPCAL1, HSPB8, ITPR3, KLF8, L1CAM, LAMA5, LIF, MYPN, NCALD, NOVA1, NTN4, PITPNC1, PITX1, PRKAA2, SCN9A, SEMA3A, SEMA4F, SEMA6D, SFRP1, SFRP2, SLC1A1, SLC22A15, SLC22A23, SLC22A4, SLC6A15, STXBP1, SYT11, TACR1, TCF7, TOR4A, TRPV2, TSPAN12, WNT16, WNT5B, ZFAND5	ADRB2, ATXN7L1, BDKRB1, CCRL1, CD9, CDH6, CELF2, COL13A1, COL4A5, DCBLD2, DUSP4, DUSP5, DUSP6, EDNRB, EHD1, FOSL1, FZD8, GABBR2, GPR39, GPR56, HPCAL1, HSPB8, IGF2BP3, ITPR3, LAMA3, LAMA5, LIF, LOXL4, MYPN, NOVA1, NTN4, PAX3, PCDH9, PITX1, SCN9A, SEMA4F, SEMA6D, SFRP1, SFRP2, SLC1A1, SLC1A2, SLC22A23, SLC22A4, SLC6A15, SLC6A6, TACR1, TC2N, TCF7, TOR4A, TRPV2, TSPAN12, WNT16, WNT5B, ZFR	Pattern specification process (GO:0007389)	3	4
								System process (GO:0003008)	46	43
Reproduction (GO:0000003)	20	13	3.5	2.7	Fertilization (GO:0009566)	ADAM15		Fertilization (GO:0009566)	1	
					Gamete generation (GO:0007276)	BMP2, CCNB1, CCND1, CCND3, CD151, CD9, CD97, DNAJB14, DNAJB9, GPR125, GPR56, PRKAA2, PSPC1, RIPK3, TSPAN12, TSPAN13, USP36	BMP2, CCND1, CCNE2, CD9, GPR56, LIMK1, RIPK3, TSPAN12, TSPAN13, ZFR	Female gamete generation (GO:0007292)	2	3
								Spermatogenesis (GO:0007283)	10	4
Response to stimulus (GO:0050896)	85	81	15.5	17.7	Cellular defense response (GO:0006968)	CXCL11, CXCL5, ETS2, ETV1, MICA, POLM, RAET1G, SH2B3, SPRY4, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21	ARHGAP20, CD163L1, CXCL11, CXCL5, ETS2, ETV1, F3, IL12A, LOXL4, SH2B3, SH2D5, SPRYD4, SQSTM1, TNFRSF1B, TNFRSF21	Cellular defense response (GO:0006968)	13	15

Contd...

Appendix Table 1: Contd...

Biological process (up-regulated)	Number of genes		Percent of gene hit against total (%)		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Defense response to bacterium (GO:0042742)	COLEC12, SCARA5	COLEC12, SCARA5	Defense response to bacterium (GO:0042742)	2	2
					İmmune response (GO:0006955)	ADRB2, ATL1, CCL26, CCL5, CD55, CD97, CLEC2B, COL10A1, CXCL11, CXCL5, ETS2, ETV1, GPR125, GPR56, IL13RA2, IL24, KLF4, KLF8, MASP1, MICA, NPTX1, POLM, RAET1G, SH2B3, TNFRSF10A, TNFRSF10D, TNFRSF1B, TNFRSF21	ADRB2, ATL1, CCL5, CCRL1, CLEC2B, COL10A1, CSF2, CXCL11, CXCL5, ETS2, ETV1, F3, GPR56, IL12A, IL13RA2, NPTX1, SH2B3, TNFRSF1B, TNFRSF21, ZFR	B cell-mediated immunity (GO:0019724)	14	7
								Complement activation (GO:0006956)	3	1
								Natural killer cell activation (GO:0030101)	1	3
								Response to interferon-gamma (GO:0034341)	1	3
					Response to endogenous stimulus (GO:0009719)	DUSP6	DUSP6, SMURF2	Response to endogenous stimulus (GO:0009719)	1	2
					Response to external stimulus (GO:0009605)	CD151, CD46, CD55, CD9, CUZD1, CXCL5, DCBLD2, F8, PAMR1, PLAT, PROCR, TFPI2, TSPAN12, TSPAN13	CD9, CXCL5, DCBLD2, F3, PAMR1, PLAT, PROCR, TFPI, TFPI2, TSPAN12, TSPAN13	Blood coagulation (GO:0007596)	12	10
					Response to stress (GO:0006950)	CD97, CREM, DNAJA3, DNAJB14, DNAJB9, DUSP10, EDNRB, GPR125, GPR39, GPR56, GPX3, HSPA5, HSPB8, HYOU1, ITPR3, LIF, NPTX1, NR4A2, PGF, PPARG, PRKAA2, RIPK3, SOD3, TACR1, VEGFA, VEGFC	ANKRD22, BDKRB1, EDNRB, GPR39, GPR56, HSPB8, IER3, ITPR3, LIF, LIMK1, NPTX1, PGF, PPARG, RIPK3, SOD3, STIP1, TACR1, VEGFC	Response to stress (GO:0006950)	26	18
					Response to toxic substance (GO:0009636)	ABHD6, GPX3		Response to toxic substance (GO:0009636)	2	

Appendix Table 2: Down-regulated transcripts and biological, ontology-based analyses in triethylene glycol dimethacrylate-treated dental pulp cells

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Apoptotic process (GO:0006915)	32	33	4.4	3,9	Induction of apoptosis (GO:0006917)	CACUL1, CNTN3, FOS, MXRA5, NEXN, RSF1, STK17B, TNFSF10, TNS3, TRAF5, VCAM1	BOC, CACUL1, DAPK1, FAF2, FOS, MXRA5, NEXN, RSF1, TRAF5, VCAM1	Induction of apoptosis (GO:0006917)	11	10
					Negative regulation of apoptotic process (GO:0043066)	AKT3, IL6, IL7, LOX, MDM2, STAT1, STAT2, ZFHX3	FAM195B, FHL1, IL7, LMO4, LOX	Negative regulation of apoptotic process (GO:0043066)	8	5
Biological adhesion (GO:0022610)	88	100	12.2	11,8	Cell adhesion (GO:0007155)	ADAMTS1, ADAMTS2, ADAMTS5, ALCAM, ANGPT1, ANGPTL1, ASPN, BGN, BMP1, C1QTNF5, CADM1, CNTN3, COL11A1, COL12A1, COL14A1, COL15A1, COL16A1, COL1A1, COL27A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CTGF, CTHRC1, DCN, ECM2, EDIL3, FAT1, FLRT2, FMOD, FNDC3B, GPC6, HEPH, HMCN1, ICAM1, ITGA11, ITGA8, ITGB8, ITGBL1, JUP, KIRREL3, KRAS, LAMA2, LOX, LRRC15, LRRC17, LRRC3, LUM, MCAM, MEGF8, MFAP4, MXRA5, NEDD9, NEGR1, NETO2, NEXN, NRAS, NRP2, NTM, NTN1, OMD, PALLD, PAPPA, PDGFD, PKP4, PODNL1, POSTN, PPFIA1, RRAS2, SDC2, SIPA1L1, SLIT2, SLITRK6, SPEG, SVEP1, TENM2, TENM3, TLR3, TNFAIP6, TNS3, VCAM1, VCAN, VIT, VWCE	ADAMTS1, ADAMTS12, ADAMTS3, ADAMTS5, ADAMTS9, ALCAM, ANGPT1, ARHGEF2, ASAP3, ASPN, BGN, BMP1, BOC, C1QTNF5, CADM1, CDC42BPA, CFB, CNTNAP1, COL11A1, COL12A1, COL14A1, COL15A1, COL1A1, COL1A2, COL27A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CTGF, CTHRC1, DAPK1, DCN, DIRAS3, ECM2, EDIL3, FLRT2, FMOD, FNDC3B, FYN, GPC6, HEPH, HMCN1, ICAM1, ITGA11, ITGA7, ITGB8, ITGBL1, JAG1, JAK1, JUP, KIRREL3, KRAS, LAMA2, LEPRE1, LIN7A, LOX, LRIG3, LRRC15, LRRC17, LSAMP, LUM, MCAM, MEGF8, MFAP4, MXRA5, NEDD9, NEGR1, NEXN, NRP2, NTM, NTN1, OBSL1, OMD, PALLD, PAPLN, PAPPA, PCOLCE, PDGFD, PKP4, PODN, POSTN, PPFIA1, RASD1, SDC2, SIPA1L1, SLIT3, SMAP1, SPEG, TENM2, TENM3, TLR3, TNFAIP6, VCAM1, VCAN, VIT, VWCE	Cell-cell adhesion (GO:0016337)	46	50
								Cell-matrix adhesion (GO:0007160)	19	21

Contd...

Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Biological regulation (GO:0065007)	155	184	21.5	21,8	Homeostatic process (GO:0042592)	ATP10A, ATP2B4, COL11A1, COL15A1, COL16A1, COL1A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2	ATP2B4, COL11A1, COL15A1, COL1A1, COL1A2, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, EDNRA	Cellular calcium ion homeostasis (GO:0006874)	2	1
								Cellular glucose homeostasis (GO:0001678)		1
								regulation of liquid surface tension (GO:0050828)	11	11
					Regulation of biological process (GO:0050789)	ADM, AFF3, AJUBA, AKT3, ATRX, BCL11A, BCLAF1, CBX5, CCNL1, CEBPD, CHD3, CHD4, CLIC4, CREB1, EGR1, EGR2, EGR3, ELF1, ETV6, ETV7, FLI1, FOS, FOXO3, FOXP1, GLI2, GNAQ, ID4, IFI16, IL6, IL7, IRF7, IRX3, JDP2, JMJD1C, JUN, JUP, KCNT2, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, KRCC1, LDB2, LOX, MAF, MAFB, MDM2, MEF2C, MEOX1, MGA, MME, MSX2, NFAT5, NR3C2, NR4A1, PDGFA, PDLIM1, PEAR1, PHC1, PPARGC1A, PRDM1, PRRX1, PSD3, RASAL2, RGS12, RSF1, RUNX1T1, RUNX2, RYBP, SCML1, SERPINF1, SERPINH1, SIX1, SKI, SLIT2, SLITRK6, SMAD6, SOX4, SP100, SP110, STAT1, STAT2, TAC1, TBX3, TCF4, TCF7L2, TOX, TSC22D3, VDR, ZBTB20, ZBTB38, ZFHX3, ZFP91, ZNF148, ZNF22, ZNF24, ZNF462, ZNF711, ZNFX1, ZSCAN31	ADM, ADM2, AFF3, AJUBA, ATF3, ATF4, ATRX, BARX1, BCL11A, BCLAF1, CBX5, CCNL1, CEBPG, CHD3, CHD4, CLIC3, CLIC4, CREB1, DDX3Y, DDX43, DUSP1, EDNRA, EGR1, EGR2, EGR3, EIF2S3, EIF4G1, EIF5, ELF1, ELF2, ETV6, FAM195B, FHL1, FLI1, FOS, FOXC1, FOXO3, FOXP1, FZD4, GLI2, GLI3, GNAI2, GNAQ, GSC, HMGB1, HR, ID4, IFI16, IL7, IRX3, JAG1, JDP2, JUP, KCNT2, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, KRCC1, LDB2, LMO4, LOX, MAF, MAFB, MEF2C, MME, NCOA1, NFAT5, NR3C1, NR4A1, NR4A3, PDGFA, PDLIM1, PEAR1, PHC1, PPARGC1A, PRDM1, PRRX1, PSD3, PTGIS, RASAL2, RGS2, RGS4, RGS5, RSF1, RUNX1T1, RUNX2, RYBP, SATB1, SCML1, SERPINB9, SERPINF1, SERPINH1, SIX1, SKI, SLIT3, SMAD6, SMARCA1, SMO, SOX4, SP110, TBX3, TCF4, TCF7L1, TCF7L2, TEAD2, TOX, TRPS1, TSC22D3, TWIST1, WNT5A, ZBTB20, ZBTB38, ZNF148, ZNF22, ZNF462, ZNF618, ZNF711, ZNFX1, ZSCAN31	Negative regulation of apoptotic process (GO:0043066)	8	5
								Regulation of nucleobase-containing compound metabolic process (GO:0019219)	87	96
								regulation of phosphate metabolic process (GO:0019220)	4	7
								Regulation of translation (GO:0006417)	1	7
								Regulation of vasoconstriction (GO:0019229)	3	5

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Regulation of molecular function (GO:0065009)	ABI2, ADAMTS1, ADAMTS2, ADAMTS5, AKAP9, BMP1, CARD16, CASP1, CCDC102B, CCNJL, CCNL1, CDKN1C, CDKN2B, CEP68, CHN1, CSTA, EDIL3, FBLIM1, FNDC3B, GAPVD1, GNAQ, HEPH, ITIH5, ITSN2, LPP, MYH10, MYH11, MYO1D, MYO6, NAP1L3, NETO2, NRP2, PDGFA, PDGFD, PDP1, PHACTR2, PPM1H, PPP1R12A, PPP1R14A, PSD3, RASAL2, RGS12, RUFY3, SEL1L3, SERPINF1, SERPINH1, SIPA1L1, STAU2	ADAMTS1, ADAMTS12, ADAMTS3, ADAMTS5, ADAMTS9, ADARB1, AKAP9, ARHGAP28, ARHGAP5, ARHGEF2, ASAP3, BIRC6, BMP1, CCDC102A, CCNJL, CCNL1, CDKN1C, CEP68, CHN1, CNTNAP1, CSTA, EDIL3, FARP1, FBLIM1, FNDC3B, GAPVD1, GNAI2, GNAQ, HEPH, ITIH5, ITSN2, LRRC8B, MYH10, MYH11, MYO6, NAP1L3, NRP2, OBSL1, PAPLN, PCOLCE, PDGFA, PDGFD, PPP1R12A, PPP1R14A, PSD3, RALBP1, RASAL2, RASSF4, RGS2, RGS4, RGS5, RIMS3, RNASE4, RUFY3, SEL1L3, SERPINB9, SERPINF1, SERPINH1, SESTD1, SIPA1L1, SLPI, SMAP1	Regulation of catalytic activity (GO:0050790)	48	62
Cellular component organization or biogenesis (GO:0071840)	70	74	9.7	8,8	Cellular component biogenesis (GO:0044085)	ADD3, HSPH1, NLGN4Y, WASF2	ADD3, HSPA5, WASF1, WASF2	Protein complex biogenesis (GO:0070271)	3	4
					Cellular component organization (GO:0016043)	ACTA2, ACTR2, AKT3, ATRX, C1QTNF5, CALD1, CBX5, CCDC102B, CHD3, CHD4, COL11A1, COL15A1, COL16A1, COL1A1, COL27A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CTHRC1, DMD, DSP, DST, DYNC1H1, DYNC1LI2, EZR, FAT1, FBLIM1, FRMD4A, ING3, JUP, KIF6, KRT7, LIMA1, LMOD1, LPP, MX1, MX2, MYH10, MYH11, MYO1D, MYO6, NAP1L3, NLGN4Y, OLFML3, PDLIM1, PHACTR2, RDX, RUNX1T1, SETBP1, SMC3, SORBS2, SP100, SP110, SPTBN1, SYNPO2, TLN1, TOX, TPM1, TPM4, TUBA1A, TUBB2A, WISP1, ZFHX3	ACTA2, ACTG2, ACTR2, ANK2, ATRX, BAZ2B, BRD4, C1QTNF5, CALD1, CBX5, CCDC102A, CDC42BPA, CHD3, CHD4, COL11A1, COL15A1, COL1A1, COL1A2, COL27A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CTHRC1, DBN1, DMD, DSP, DST, DYNC1H1, DYNC1LI2, EZR, FBLIM1, FHL1, FOXC1, HMGB1, ING3, JUP, KRT7, LIMA1, LIN7A, LMO4, LMOD1, MKNK2, MYH10, MYH11, MYO6, NAP1L3, OLFML2A, OLFML3, PDLIM1, RUNX1T1, SETBP1, SETD8, SMARCA1, SMC3, SMC4, SORBS2, SP110, SYNPO2, TLN1, TOP1, TOP2A, TOX, TPM1, TUBE1, WISP1, ZAK	Cellular component morphogenesis (GO:0032989)	46	44
								Organelle organization (GO:0006996)	13	20

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Cellular process (GO:0009987)	332	371	46.0	43,9	Cell communication (GO:0007154)	ABI2, ADAMTS1, ADAMTS2, ADAMTS5, AFF3, AKT3, ALCAM, ALPK2, ANGPT1, ANGPTL1, ASPN, BGN, BMP1, BMP4, BMPR2, CACNA1C, CADM1, CAP2, CCDC102B, CDK11A, CDK6, CEP68, CHN1, CHRNA9, CLIC4, CNTN3, COL11A1, COL15A1, COL16A1, COL1A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CREB1, CTGF, CTHRC1, CXCL1, CXCL10, CXCL6, CXCR7, DCN, DTX3L, DYNC1LI2, EDIL3, EFNB2, ELF1, ETV6, ETV7, FABP3, FAT1, FBN1, FBN2, FER, FGF1, FGF7, FLI1, FLRT2, FNDC3B, FOXO3, GADD45B, GDF5, GHR, GNAQ, GNG12, GPR124, GPR133, GPR183, GRIA3, HEPH, HTRA1, IFI35, IL6, IL6ST, IL7, INHBA, INHBE, ITGB8, ITGBL1, ITSN2, JUN, JUP, KCNMB1, KRAS, LAMA2, LEPR, LIMS2, LOX, LPHN2, LPPR4, LRRC15, LRRC17, LRRC3, LTBP2, MARCKS, MCAM, MEGF8, MFAP4, MME, MORN2, MXRA5, MYH10, MYH11, MYO1D, MYO6, NETO2, NMI, NR3C2, NR4A1, NRAS, NRP2, NTN1, OLFML3, PAPPA, PDE7B, PDGFA, PDGFD, PDP1, PEAR1, PHLDB2, PKN2, PKP4, PLXNA2, PLXNC1, PLXND1, PODNL1, POSTN, PPAP2B, PPM1H, PRKCI, PRKG1, PTGDS, PTGER2, PTGER4, PTGFR, PTK7, PTN, PTPLA, PTPRD, PXK, RASAL2, RCAN2, RHOBTB1,	ACVR2A, ADAMTS1, ADAMTS12, ADAMTS3, ADAMTS5, ADAMTS9, AFF3, ALCAM, ALPK2, ANGPT1, ARHGEF2, ASAP3, ASPN, BGN, BMP1, BMP4, BMPR2, BOC, CADM1, CAP2, CBLB, CCDC102A, CDC42BPA, CDK11A, CDK6, CEP68, CFB, CHN1, CHRNA1, CLIC3, CLIC4, CNTNAP1, COL11A1, COL15A1, COL1A1, COL1A2, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CREB1, CTGF, CTHRC1, CXCL6, CXCR7, CYSLTR1, DCN, DEPDC1, DIRAS3, DYNC1LI2, EDIL3, EDNRA, EFNB2, ELF1, ELF2, ETV6, FAF2, FAM195B, FBN1, FBN2, FER, FGF1, FGF7, FLI1, FLRT2, FNDC3B, FOXC1, FOXO3, FYN, FZD4, GNAI2, GNAQ, GNG12, GNG2, GPCPD1, GPR124, GPR133, GPR183, GPR64, GRIA3, HEPH, HMGB1, HTRA1, IL11RA, IL20RB, IL6ST, IL7, INHBA, INHBE, IRAK3, ISLR, ITGB8, ITGBL1, ITSN2, JAG1, JAK1, JUP, KRAS, KREMEN1, LAMA2, LEPR, LEPRE1, LIMS2, LOX, LPHN2, LPPR4, LRIG3, LRRC15, LRRC17, LRRC8B, LTBP1, LTBP2, LTBP4, MARCKS, MCAM, MEGF10, MEGF8, MFAP4, MIB1, MKNK2, MME, MXRA5, MYH10, MYH11, MYO6, NCOA1, NR3C1, NR4A1, NR4A3, NRP2, NTN1, OBSL1, OLFML2A, OLFML3, PAPLN, PAPPA, PCOLCE, PDE4B, PDE4D, PDE7B, PDGFA, PDGFD, PEAR1, PHLDB2, PIM1, PKN2, PKP4, PLXNA4, PLXNC1, PLXND1, PODN, POSTN, PPAP2B, PPP2R5E, PRKCI, PRKG1, PTGDS, PTGER2, PTGER4, PTGFR, PTK7, PTN, PTPRD, PXK, RASAL2, RASD1, RASSF4, RCAN1, RHOA, RHOBTB1, RHOBTB3, RHOQ,	Cell-cell signaling (GO:0007267)	46	47

Contd...

Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
						RHOBTB3, RHOQ, RRAS2, RUFY3, RUNX2, S1PR1, SCG5, SDC2, SEMA3C, SH3PXD2A, SKI, SLC1A3, SLIT2, SLITRK6, SMAD6, SNTB1, SNTB2, SORBS2, SP100, SP110, SPARC, STAT1, STAT2, SV2A, SVEP1, SYNJ2BP, TAC1, TACSTD2, TCF7L2, TENM2, TENM3, TGFB2, TLR3, TMTC1, TNFAIP6, TNFSF10, TNFSF4, TNS3, TOX, TRAF5, VCAM1, WISP1, WNK1	RIMS3, RPS6KA2, RUFY3, RUNX2, S1PR1, SCG5, SDC2, SEMA3C, SEMA3D, SESTD1, SH3PXD2A, SKI, SLC1A3, SLC1A4, SLC6A9, SLIT3, SMAD6, SMAP1, SMO, SNTB1, SNTB2, SORBS2, SP110, SPARC, SV2A, TCF7L1, TCF7L2, TENM2, TENM3, TGFB2, TGFB3, TLR3, TMTC4, TNFAIP6, TOX, TRAF5, TRIB2, TRIB3, TRPC6, UNC5D, VCAM1, WISP1, WNK1, WNT5A, WSB1, ZAK, ZFP36L1			
					Cell cycle (GO:0007049)	ABI2, ACTA2, ACTR2, AKT3, BICC1, CACUL1, CALD1, CCDC102B, CCNJL, CCNL1, CDK11A, CDK6, CDKN1C, CDKN2B, CNTN3, CTGF, DDX60L, DKC1, DNAJC1, DYNC1H1, DYNC1LI2, EGR1, EGR2, EGR3, EIF2AK2, ELF1, ETV6, ETV7, FBLIM1, FGF7, FLI1, FOS, GADD45B, IGF2, ING3, JDP2, JUN, KIF6, LPP, MAF, MAFB, MXRA5, MYH10, MYH11, MYO1D, MYO6, NAP1L3, NDN, NEDD9, NUCKS1, PHC1, PRKG1, PTK7, RAD1, RAD21, RBM24, RBMS1, RBMS3, REV1, RFC5, RSF1, SCML1, SMC3, STAG2, STAU2, SYNCRIP, TNS3, TUBA1A, TUBB2A, UBE2J1, VCAM1, WISP1, ZNFX1	ACTA2, ACTG2, ACTR2, ADARB1, ARHGEF2, ATF3, BICC1, BOC, CACUL1, CALD1, CCDC102A, CCNJL, CCNL1, CDC42BPA, CDK11A, CDK6, CDKN1C, CTGF, DKC1, DNAJC1, DYNC1H1, DYNC1LI2, EGR1, EGR2, EGR3, ELF1, ELF2, ETV6, FAM179B, FBLIM1, FGF7, FLI1, FOS, IGF1, IGF2, ING3, JDP2, MAF, MAFB, MXRA5, MYH10, MYH11, MYO6, NAP1L3, NDN, NEDD9, NUCKS1, PHC1, PMP22, PRKG1, PTK7, RAD1, RAD21, RALBP1, RBM47, RBMS1, RBMS3, REV1, RPS6KA2, RSF1, SCML1, SESN2, SESN3, SMC3, SMC4, STAG2, SYNCRIP, TOP2A, TUBE1, UBE2J1, VCAM1, WISP1, ZAK, ZFP36L1, ZNFX1	Meiosis (GO:0007126) Mitosis (GO:0007067)	3 27	3 28
					Cell proliferation (GO:0008283)	FER, FOXO3, FOXP1, PDGFA	FER, FOXC1, FOXO3, FOXP1, FYN, JAK1, PDGFA	Cell proliferation (GO:0008283)	4	7

Contd...

Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Cellular component movement (GO:0006928)	ABI2, CCDC102B, COL12A1, COL14A1, CTGF, DAAM2, DMD, DOK6, DSP, DST, DYNC1H1, FAT1, FBLIM1, KIAA1598, LIMA1, LIMS2, LMCD1, LPP, MYH10, MYH11, MYO1D, MYO6, PDGFA, PDLIM1, SLIT2, SLITRK6, SPTBN1, SYNPO2, TPM1, TPM4, TUBA1A, TUBB2A, VIT, WISP1, ZFHX3	CCDC102A, CDC42BPA, COL12A1, COL14A1, CTGF, DMD, DOK6, DSP, DST, DYNC1H1, FBLIM1, FHL1, JAG1, LIMA1, LIMS2, LMCD1, LMO4, MYH10, MYH11, MYO6, PDGFA, PDLIM1, PRICKLE1, SLIT3, SYNPO2, TPM1, TUBE1, VIT, WISP1	Cellular component movement (GO:0006928)	35	29
					Chromosome segregation (GO:0007059)	BICC1, DYNC1H1, KIF6, RAD21, REV1, SMC3, STAG2, TUBA1A, TUBB2A, UBE2J1	BICC1, DYNC1H1, RAD21, REV1, SMC3, SMC4, STAG2, TOP2A, TUBE1, UBE2J1	Chromosome segregation (GO:0007059)	10	10
					Cytokinesis (GO:0000910)	ACTA2, ACTR2, CCDC102B, KIF6, MYH10, MYH11, MYO1D, MYO6	ACTA2, ACTG2, ACTR2, CCDC102A, MYH10, MYH11, MYO6	Cytokinesis (GO:0000910)	8	7
Developmental process (GO:0032502)	205	218	28.4	25,8	Anatomical structure morphogenesis (GO:0009653)	ACTA2, AKT3, C1QTNF5, CALD1, CCDC102B, COL11A1, COL15A1, COL16A1, COL1A1, COL27A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CTHRC1, DMD, DSP, DST, DYNC1LI2, EZR, FAT1, FBLIM1, FOXO3, FOXP1, FRMD4A, HMCN1, JUP, KRT7, LIMA1, LMOD1, LPP, MYH10, MYH11, OLFML3, PALLD, PDLIM1, PHACTR2, RDX, SORBS2, SPEG, SPTBN1, SYNPO2, TLN1, TPM1, TPM4, TUBA1A, TUBB2A, WISP1, ZFHX3	ACTA2, ACTG2, ANK2, C1QTNF5, CALD1, CCDC102A, CDC42BPA, COL11A1, COL15A1, COL1A1, COL1A2, COL27A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CTHRC1, DBN1, DMD, DSP, DST, DUSP1, DYNC1LI2, EZR, FBLIM1, FHL1, FOXC1, FOXO3, FOXP1, HMCN1, JUP, KRT7, LIMA1, LIN7A, LMO4, LMOD1, MYH10, MYH11, OLFML2A, OLFML3, PALLD, PDLIM1, SORBS2, SPEG, SYNPO2, TLN1, TPM1, WISP1	Cellular component morphogenesis (GO:0032989)	46	44
					Cell differentiation (GO:0030154)	FOXO3, FOXP1, JUP, PSD3, TCF7L2	FOXC1, FOXO3, FOXP1, FYN, JAK1, JUP, PSD3, TCF7L1, TCF7L2, WNT5A	Cell differentiation (GO:0030154)	5	10

Contd...

Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Death (GO:0016265)	ADAM12, ADAM19, AKT3, CACUL1, CARD16, CASP1, CBX5, CNTN3, FOS, GADD45B, HTRA1, IL6, IL7, KRCC1, LOX, MAGED4, MDM2, MXRA5, NAP1L3, NDN, NEXN, RSF1, SKI, STAT1, STAT2, STAU2, STK17B, TNFSF10, TNS3, TRAF5, VCAM1, ZFHX3	ADAM12, ADAM19, ADARB1, ADH1B, ARHGEF2, BOC, CACUL1, CBX5, DAPK1, DUSP1, EIF4G1, FAF2, FAM195B, FHL1, FOS, FYN, HTRA1, IL7, JAK1, KRCC1, LMO4, LOX, MAGED4, MXRA5, NAP1L3, NDN, NEXN, RASSF4, RSF1, SKI, TRAF5, UNC5D, VCAM1	Cell death (GO:0008219)	32	33
					Ectoderm development (GO:0007398)	ADAMTS1, ALCAM, BMP1, BMP4, BNC1, BNC2, CDK6, CHRNA9, CNTN3, COL11A1, COL15A1, COL16A1, COL1A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CREB1, EDIL3, EFNB2, FABP3, FAT1, GDF5, GLI2, HEPH, HSPG2, INHBA, INHBE, IRX3, LAMA2, MAML2, MCAM, MEGF8, MXRA5, NEGR1, NETO2, NR4A1, NRP2, NTM, NTN1, OLFML3, PDGFD, PEAR1, PHC1, POGZ, PPFIA1, PRRX1, PTK7, RBM24, RBMS1, RBMS3, RTN4, RUNX2, SCML1, SEMA3C, SLIT2, SLITRK6, SYNCRIP, TCF4, TENM2, TENM3, TGFB2, TPM1, TPM4, VCAM1, VCAN, ZFHX3	ADAMTS1, ALCAM, BARX1, BMP1, BMP4, BNC1, BNC2, BOC, CDK6, CHRNA1, CNTNAP1, COL11A1, COL15A1, COL1A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CREB1, EDIL3, EDNRA, EFNB2, FHL1, GLI2, GLI3, GSC, HEPH, HSPG2, IFRD1, INHBA, INHBE, IRX3, JAG1, LAMA2, LMO4, LSAMP, MCAM, MEGF8, MXRA5, NEGR1, NR4A1, NR4A3, NRP2, NTM, NTN1, OLFML2A, OLFML3, PCOLCE, PDGFD, PEAR1, PHC1, POGZ, PPFIA1, PRRX1, PTK7, RBM47, RBMS1, RBMS3, RPS6KA2, RUNX2, SCML1, SEMA3C, SEMA3D, SLIT3, SYNCRIP, TCF4, TENM2, TENM3, TGFB2, TGFB3, TPM1, UNC5D, VCAM1, VCAN	Ectoderm development (GO:0007398)	69	76
					Embryo development (GO:0009790)	CDK6, FAT1, GLI2, JUP, MEF2C, PTK7, RUNX2, VGLL3, ZFHX3	CDC42BPA, CDK6, DUSP1, FHL1, FOXC1, GLI2, GLI3, JUP, LMO4, MEF2C, PTK7, RUNX2	Embryo development (GO:0009790)	9	12
					Endoderm development (GO:0007492)	ELF1	DUSP1, ELF1, ELF2, TRPS1	Endoderm development (GO:0007492)	1	4

Contd...

Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Mesoderm development (GO:0007498)	ADAM12, ADAM19, ADAMTS1, ASPN, BGN, BMP1, BMP4, BMPR2, C1QTNF5, CCDC102B, CDH11, CDH13, CDH6, CDK6, CEBPD, CNTN3, COL11A1, COL15A1, COL16A1, COL1A1, COL27A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CTGF, CTHRC1, DCN, EDIL3, EFHD1, ELF1, ETV6, ETV7, FBN1, FBN2, FGF7, FLI1, FLRT2, FNDC3B, FOS, GDF5, GPR124, GPR133, HEPH, HMCN1, INHBA, INHBE, KIRREL3, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, LPHN2, LRRC15, MEF2C, MEOX1, MGA, MIER1, MSX2, MXRA5, MYH10, MYH11, NETO2, NFE2L2, NFE2L3, NRP2, OXTR, PALLD, PCDH7, PCDH9, PDGFD, PDLIM1, PHC1, PHLDB2, PODNL1, POSTN, PRRX1, PTK7, RUNX2, SCML1, SEMA3C, SPEG, STAT1, STAT2, TBX3, TENM2, TENM3, TGFB2, TPM1, TPM4, TRAF5, VCAM1, VCAN, VDR, WISP1, ZFHX3, ZHX2	ACVR2A, ADAM12, ADAM19, ADAMTS1, ASPN, BARX1, BCL9L, BGN, BMP1, BMP4, BMPR2, BOC, C1QTNF5, CCDC102A, CDH11, CDH13, CDK6, CEBPG, CNTNAP1, COL11A1, COL15A1, COL1A1, COL27A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CTGF, CTHRC1, DCN, EDIL3, EFHD1, ELF1, ELF2, ETV6, FARP1, FBN1, FBN2, FGF7, FHL1, FLI1, FLRT2, FNDC3B, FOS, FOXC1, GPR124, GPR133, GPR64, GSC, HEPH, HMCN1, INHBA, INHBE, KIRREL3, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, LMO4, LPHN2, LRRC15, MEF2C, MXRA5, MYH10, MYH11, MYL9, NFE2L1, NFE2L2, NFE2L3, NRP2, OBSL1, OXTR, PALLD, PCDH7, PCOLCE, PDGFD, PDLIM1, PHC1, PHLDB2, PODN, POSTN, PRRX1, PTK7, RNASE4, RPS6KA2, RUNX2, SCML1, SEMA3C, SEMA3D, SPEG, TBX3, TENM2, TENM3, TGFB2, TGFB3, TPM1, TRAF5, TRPS1, TWIST1, VCAM1, VCAN, WISP1, WSB1, ZHX2	Digestive tract mesoderm development (GO:0007502)	2	1
					Pattern specification process (GO:0007389)	CDK6, GLI2, JUP, KLF12, KLF13, KLF9, PRRX1, STAU2, TENM2, TENM3	ADARB1, CDK6, FOXC1, GLI2, GLI3, GSC, JUP, KLF12, KLF13, KLF9, OSR2, PRRX1, TENM2, TENM3	Anterior/posterior axis specification (GO:0009948)	6	6
								Segment specification (GO:0007379)	3	6

Contd...

Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Sex determination (GO:0007530)	RUNX2, TCF4	RUNX2, TCF4	Sex determination (GO:0007530)	2	2
					System development (GO:0048731)	ADAM12, ADAM19, ADAMTS1, ALCAM, AMOT, ANGPT1, ANGPTL1, ASPN, BGN, BMP1, BMP4, BMPR2, BNC1, BNC2, C1QTNF5, CCDC102B, CDH11, CDH13, CDH6, CDK6, CEBPD, CHRNA9, CNTN3, CREB1, CSRP2, CTGF, CTHRC1, CXCL1, CXCL10, CXCL6, DCN, EDIL3, EFHD1, EFNB2, ELF1, EPHA3, ETV6, ETV7, FAT1, FBLIM1, FBN1, FBN2, FGF7, FLI1, FLRT2, FNDC3B, FOS, FOXO3, FOXP1, GDF5, GHR, GLI2, GPR124, GPR133, HEPH, IL6ST, IL7R, INHBA, INHBE, IRX3, JUP, KIRREL3, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, LAMA2, LEPR, LMOD1, LPHN2, LPP, LRRC15, LTBP2, MAF, MAFB, MAML2, MCAM, MEF2C, MEOX1, MSX2, MXRA5, MYH10, MYH11, NEGR1, NETO2, NFE2L2, NFE2L3, NLGN4Y, NRP2, NTM, NTN1, OLFML3, OXTR, PALLD, PCDH7, PCDH9, PDGFD, PDLIM1, PEAR1, PHC1, PHLDB2, PLXNA2, PLXNC1, PLXND1, PODNL1, POSTN, PPFIA1, PRRX1, PSD3, RBM24, RBMS1, RBMS3, RTN4, RUNX2, SCML1, SDC2, SEMA3C, SLIT2, SLITRK6, SPEG, STAT1, STAT2, SYNPO2, TCF4, TCF7L2, TENM2, TENM3, TGFB2, TNFAIP2, TNFSF10, TPM1, TPM4, TRAF5, VCAN, VDR, WISP1, ZFHX3, ZHX2	ACVR2A, ADAM12, ADAM19, ADAMTS1, ALCAM, ANGPT1, ASPN, BARX1, BGN, BMP1, BMP4, BMPR2, BNC1, BNC2, BOC, C1QTNF5, CCDC102A, CDH11, CDH13, CDK6, CHRNA1, CNTNAP1, CREB1, CSRP2, CTGF, CTHRC1, CXCL6, DCN, EDIL3, EDNRA, EFHD1, EFNB2, ELF1, ELF2, EPHA3, EPHA4, ETV6, FARP1, FBLIM1, FBN1, FBN2, FGF7, FHL1, FLI1, FLRT2, FNDC3B, FOS, FOXC1, FOXO3, FOXP1, FZD4, GLI2, GLI3, GPR124, GPR133, GPR64, GSC, HEPH, IFRD1, IL11RA, IL6ST, INHBA, INHBE, IRX3, ITM2C, JAG1, JUP, KIRREL3, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, LAMA2, LEPR, LMO4, LMOD1, LPHN2, LRRC15, LSAMP, LTBP1, LTBP2, LTBP4, MAF, MAFB, MCAM, MEF2C, MXRA5, MYH10, MYH11, MYL9, NEGR1, NFE2L1, NFE2L2, NFE2L3, NRP2, NTM, NTN1, OBSL1, OLFML2A, OLFML3, OXTR, PALLD, PCDH7, PCOLCE, PDGFD, PDLIM1, PEAR1, PHC1, PHLDB2, PLXNA4, PLXNC1, PLXND1, PODN, POSTN, PPFIA1, PRRX1, PSD3, RBM47, RBMS1, RBMS3, RNASE4, ROR2, RPS6KA2, RUNX2, SCML1, SDC2, SEMA3C, SEMA3D, SLIT3, SMO, SPEG, SYNPO2, TCF4, TCF7L1, TCF7L2, TENM2, TENM3, TGFB2, TGFB3, TNFAIP2, TPM1, TRAF5, TRPS1, TWIST1, UNC5D, VCAN, WISP1, WNT5A, ZHX2	Angiogenesis (GO:0001525)	22	22
								Heart development (GO:0007507)	25	29
								Hemopoiesis (GO:0030097)	19	16
								Muscle organ development (GO:0007517)	34	34
								Nervous system development (GO:0007399)	65	77
								Skeletal system development (GO:0001501)	34	38

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Growth (GO:0040007)		1		0.1	Growth (GO:0040007)		FOXC1	Growth (GO:0040007)		1
Immune system process (GO:0002376)	104	99	14.4	11,7	Antigen processing and presentation (GO:0019882)	ULBP1	ULBP1	Antigen processing and presentation (GO:0019882)	1	1
					Immune response (GO:0006955)	C1QTNF5, CCL2, CCL7, CCL8, CEBPD, CXCL1, CXCL10, CXCL6, CXCR7, ELF1, ETV6, ETV7, FLI1, GBP1, GBP2, GBP5, GHR, GPR124, GPR133, IFI16, IFI35, IL6ST, IL7R, IRF7, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, LEPR, LPHN2, NMI, OAS1, OAS2, OAS3, PAPPA, PHLDB2, STAT1, STAT2, STAU2, SVEP1, SWAP70, TAC1, TNFAIP2, TNFSF10, TRIM14, ULBP1	ADARB1, C1QTNF5, C1R, CCL11, CCL2, CCL7, CCL8, CFB, CXCL6, CXCR7, ELF1, ELF2, ETV6, FLI1, GBP1, GBP5, GPR124, GPR133, GPR64, IFI16, IL11RA, IL20RB, IL6ST, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, LEPR, LPHN2, PAPPA, PHLDB2, SESTD1, TNFAIP2, ULBP1	B cell-mediated immunity (GO:0019724)	16	16
								Complement activation (GO:0006956)	3	4
								Natural killer cell activation (GO:0030101)	2	1
								Response to interferon-gamma (GO:0034341)	9	4
					Macrophage activation (GO:0042116)	CD302, COL11A1, COL15A1, COL16A1, COL1A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CXCL1, CXCL10, CXCL6, ELF1, ETV6, ETV7, FLI1, GBP1, GBP2, GBP5, LOX, PHLDB2, SDC2, TNFAIP2	CD302, COL11A1, COL15A1, COL1A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CXCL16, CXCL6, ELF1, ELF2, ETV6, FLI1, GBP1, GBP5, IL20RB, LOX, LY75, MRC2, PHLDB2, SDC2, TNFAIP2	Macrophage activation (GO:0042116)	25	25
Localization (GO:0051179)	103	113	14.3	13,4	RNA localization (GO:0006403)	DYNC1LI2, STAU2	ADARB1, DYNC1LI2	RNA localization (GO:0006403)	2	2
					Protein localization (GO:0008104)	JUP, MPDZ, RUFY3	JUP, LNX1, RUFY3	Asymmetric protein localization (GO:0008105)	2	2

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Transport (GO:0006810)	ABCA13, ABCA5, ACTA2, ACTR2, AKAP9, AP3B1, ATP10A, ATP1B1, ATP2B4, BICC1, BMP1, CACNA1C, CCDC102B, CD302, CEP68, CHRNA9, CLIC4, COL11A1, COL15A1, COL16A1, COL1A1, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, COPZ2, DYNC1H1, DYNC1LI2, EDIL3, EXOC6, FABP3, GAPVD1, GJC1, GPR124, GPR133, GRIA3, HEPH, IGF2, ITSN2, KCNE3, KCNK1, KCNK2, KCNMB1, KCNT2, KCTD15, KIF6, KRAS, LAMP3, LOX, LPHN2, MPDZ, MX1, MX2, MYH10, MYH11, MYO1D, MYO6, NETO2, NRAS, NRP2, OLFML3, OSBPL8, PAPPA, PDGFD, PEAR1, PLSCR1, PPIC, PPP1R14A, PTGDS, PTGER2, PTGER4, PTGFR, PTK7, RAMP1, RHOBTB1, RHOBTB3, RHOQ, RRAS2, RTN4, RUFY3, SAA1, SEC14L1, SHROOM2, SLC1A3, SLC2A12, SLC38A1, SLC38A4, SNX18, SNX3, SORBS2, SORT1, SVEP1, SYNJ2BP, TNFAIP2, TUBA1A, TUBB2A, USO1	ACTA2, ACTG2, ACTR2, AKAP9, AP3B1, APOL6, AQP1, ARHGEF2, ARL6IP1, ATP2B4, BICC1, BMP1, CCDC102A, CD302, CEP68, CFB, CHRNA1, CLIC3, CLIC4, CNTNAP1, COL11A1, COL15A1, COL1A1, COL1A2, COL3A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, COPZ2, CWC27, DIRAS3, DYNC1H1, DYNC1LI2, EDIL3, GAPVD1, GPR124, GPR133, GPR64, GRIA3, HEPH, IGF1, IGF2, ITSN2, KCNE3, KCNK1, KCNK2, KCNT2, KCTD12, KCTD15, KRAS, LAMP3, LNX1, LOX, LPHN2, LY75, MRC2, MYH10, MYH11, MYO6, NKTR, NRP2, OLFML2A, OLFML3, OSBPL8, PAPPA, PCOLCE, PDGFD, PEAR1, PPIC, PPP1R14A, PTGDS, PTGER2, PTGER4, PTGFR, PTK7, RAMP1, RASD1, RHOA, RHOBTB1, RHOBTB3, RHOQ, RIMS3, RUFY3, SAA1, SEC14L1, SHROOM2, SLC1A3, SLC1A4, SLC25A36, SLC26A10, SLC2A12, SLC31A1, SLC38A1, SLC38A4, SLC39A6, SLC6A9, SNX18, SNX3, SORBS2, SORT1, TMEM176B, TNFAIP2, TRAM1, TRPC6, TUBE1, USO1, VPS35	Amino acid transport (GO:0006865)	3	6
								Carbohydrate transport (GO:0008643)	4	5
								Extracellular transport (GO:0006858)	2	4
								Ion transport (GO:0006811)	16	21
								Lipid transport (GO:0006869)	17	16
								Lysosomal transport (GO:0007041)	1	1
								Nuclear transport (GO:0051169)	1	3
								Nucleobase-containing compound transport (GO:0015931)		1
								Peroxisomal transport (GO:0043574)	2	2
								Phosphate ion transport (GO:0006817)	1	3
								Protein transport (GO:0015031)	68	74
								Vesicle-mediated transport (GO:0016192)	53	57
Locomotion (GO:0040011)	1	1	0.1	0,1	Locomotion (GO:0040011)	PDGFA	PDGFA	Locomotion (GO:0040011)	1	1

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Metabolic process (GO:0008152)	336	415	46.5	49,1	Biosynthetic process (GO:0009058)	FOXO3, GNAQ, JUP, SKI, TCF7L2	FOXC1, FOXO3, GNAI2, GNAQ, JUP, MGST2, SKI, TCF7L1, TCF7L2, TOP1, TOP2A	Biosynthetic process (GO:0009058)	5	11
					Catabolic process (GO:0009056)	GNAQ, HECW2, ITCH, PSD3, RASAL2, RGS12	GNAI2, GNAQ, ITCH, PSD3, RASAL2, RGS2, RGS4, RGS5, TOP2A	Catabolic process (GO:0009056)	6	9
					Coenzyme metabolic process (GO:0006732)	GCH1	GCH1	Coenzyme metabolic process (GO:0006732)	1	1
					Generation of precursor metabolites and energy (GO:0006091)	CYP1B1, CYP7B1, KRCC1, NOX4, PDP1, SH3PXD2A	CYP1B1, CYP7B1, ENOX1, FMO3, KRCC1, PTGIS, SH3PXD2A, YPEL2	Glycolysis (GO:0006096)	1	
								Respiratory electron transport chain (GO:0022904)	5	8
					Nitrogen compound metabolic process (GO:0006807)	AKT3, FOXO3, FOXP1, GNAQ, JUP, PSD3, RASAL2, RGS12, SKI, TCF7L2	FOXC1, FOXO3, FOXP1, GNAI2, GNAQ, GPT2, JUP, PSD3, RASAL2, RGS2, RGS4, RGS5, SKI, TCF7L1, TCF7L2, TOP1, TOP2A	Nitric oxide biosynthetic process (GO:0006809)	1	
								Porphyrin-containing compound metabolic process (GO:0006778)		1
					Phosphate-containing compound metabolic process (GO:0006796)	ABCA13, ABCA5, ACPL2, GNAQ, LPPR4, OLFML3, PDGFA, PLSCR1, PPAP2B, PSD3, RASAL2, RGS12, SULF1, SULF2, TNS3	DUSP1, GNAI2, GNAQ, LPPR4, OLFML2A, OLFML3, PDGFA, PPAP2B, PSD3, RASAL2, RGS2, RGS4, RGS5, SLC25A36, SULF1, SULF2, TOP2A, ZAK	Phospholipid metabolic process (GO:0006644)	9	4

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
								Regulation of phosphate metabolic process (GO:0019220)	4	7
					Primary metabolic process (GO:0044238)	AASS, ABCA13, ABCA5, ACPL2, ADAMTS1, ADAMTS2, ADAMTS5, ADCY9, ADD3, AFF3, AJUBA, AK5, AKT3, ALDH2, ALG11, ALPK2, ARHGEF10, ARID5B, ASNS, ATP10A, ATRX, BACE1, BACE1, BCAT1, BCL11A, BCLAF1, BICC1, BMP1, BMPR2, C7orf10, CACUL1, CAMKK2, CARD16, CASP1, CBS, CBX5, CCNL1, CDK11A, CDK6, CEBPD, CERS6, CH25H, CHD3, CHD4, CHN1, CHSY3, CLIC4, CNTN3, CPE, CREB1, CRYAB, CSTA, CYP1B1, CYP7B1, DDX60L, DHRS3, DKC1, DNAJC1, DPYSL2, DTX3L, DYNC1LI2, DZIP3, EDIL3, EGR1, EGR2, EGR3, EIF2AK2, ELF1, ELOVL2, ENPEP, EPRS, ETV6, ETV7, FABP3, FER, FKBP14, FKBP9, FLI1, FNDC3B, FOS, FOXO3, FOXP1, GCH1, GFPT2, GLI2, GNAQ, GTF2H2, GUCY1B3, GXYLT2, HAS2, HECW2, HEPH, HINT3, HMCN1, HSP90B1, HSPB3, HSPB7, HSPH1, HTRA1, ID4, IFI16, IGF2, ING3, INSIG1, IRF7, IRX3, ITCH, ITIH5, JDP2, JMJD1C, JUN, JUP, KDM4B, KIAA2018, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, KRCC1, LAMP3, LARP7, LCTL, LDB2, LEPREL4, LOX, LPPR4, LRRFIP1, MAF, MAFB, MED13L, MEF2C, MEOX1, MEST, MEX3B, MGA, MGA, MIER1, MME,	AASS, ACVR2A, ADAMTS1, ADAMTS12, ADAMTS3, ADAMTS5, ADAMTS9, ADARB1, ADD3, ADH1B, AFF3, AJUBA, ALDH1A1, ALDH1L2, ALDH2, ALG11, ALPK2, APOL6, ARG2, ARHGAP5, ARHGEF2, ARID5B, ASNS, ATF3, ATF4, ATRX, BACE1, BACE1, BARX1, BAZ2B, BCAT1, BCL11A, BCLAF1, BICC1, BMP1, BMPR2, BOC, BRD4, C1R, CACUL1, CAMKK2, CBS, CBX5, CCNL1, CDC42BPA, CDK11A, CDK6, CEBPG, CERS6, CFB, CFD, CH25H, CHD3, CHD4, CHN1, CHSY3, CLIC3, CLIC4, CNTNAP1, CPE, CPM, CREB1, CRYAB, CSTA, CTH, CTSC, CWC27, CYP1B1, CYP7B1, DAPK1, DDX3Y, DDX43, DHCR7, DHRS3, DHX36, DKC1, DNAJC1, DPYSL2, DUSP1, DYNC1LI2, DYRK2, DZIP3, EDIL3, EDNRA, EGR1, EGR2, EGR3, EIF2S3, EIF4EBP1, EIF4G1, EIF5, ELF1, ELF2, ELOVL2, ENPP1, ENTPD3, EPRS, ETV6, FAM195B, FER, FHL1, FKBP9, FLI1, FMO3, FNDC3B, FOS, FOXC1, FOXO3, FOXP1, FYN, GCH1, GFPT2, GLI2, GLI3, GNAI2, GNAQ, GPT2, GPX7, GSC, GTF2H2, GUCY1B3, GXYLT2, H6PD, HADHA, HAS2, HEPH, HMCN1, HMGB1, HR, HSP90B1, HSPA5, HSPB3, HTRA1, ID4, IFI16, IGF1, IGF2, ING3, INSIG1, IRAK3, IRX3, ISG15, ISG20, ITCH, ITIH5, JAG1, JAK1, JDP2, JHDM1D, JUP, KDM4A, KDM4B, KDM5A,	Carbohydrate metabolic process (GO:0005975)	18	22

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
						MSRB3, MSX2, MXRA5, NAP1L3, NETO2, NEXN, NFAT5, NFE2L2, NFE2L3, NFIB, NFIX, NPR3, NR3C2, NR4A1, NRP2, NSUN6, NUCKS1, OAS1, OAS2, OAS3, OGT, OSBPL8, PALLD, PAPPA, PARP14, PARP9, PDE7B, PDGFA, PDGFD, PDLIM1, PDP1, PEAR1, PHC1, PHF17, PHGDH, PKN2, PLSCR1, PLXNA2, PLXNC1, PLXND1, POGZ, PPAP2B, PPARGC1A, PPIC, PPM1H, PPP1R12A, PPP1R14A, PRDM1, PRKCI, PRKG1, PRMT2, PRRX1, PSAT1, PSD3, PTGDS, PTK7, PTPN11, PTPN13, PTPRD, PTPRO, RAD1, RAD21, RAD23B, RASAL2, RBM17, RBM24, RBMS1, RBMS3, REV1, RFC5, RGS12, RNF144B, RPL27A, RSF1, RUFY3, RUNX1T1, RUNX2, RYBP, SCD, SCML1, SEC14L1, SERBP1, SERPINF1, SERPINH1, SETBP1, SIX1, SKI, SLC1A3, SLC2A12, SLC38A1, SLC38A4, SLIT2, SLITRK6, SMAD6, SMC3, SORBS2, SORT1, SOX4, SP100, SP110, SPEG, STAT1, STAT2,	KIAA2018, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, KRCC1, LAMP3, LARP7, LCTL, LDB2, LMO4, LOX, LPPR4, LRRC8B, LRRFIP1, MAF, MAFB, MARS, MBD4, MED13, MED13L, MEF2C, MEST, MEX3B, MGST2, MIB1, MID2, MKNK2, MME, MSRB3, MXRA5, NAP1L3, NCOA1, NEXN, NFAT5, NFE2L1, NFE2L2, NFE2L3, NFIB, NFIC, NKTR, NME5, NPR3, NR3C1, NR4A1, NR4A3, NRP2, NSUN6, NUCKS1, OBSL1, OGT, OSBPL8, OSR2, PALLD, PAPLN, PAPPA, PCK2, PCOLCE, PDE4B, PDE4D, PDE7B, PDGFA, PDGFD, PDLIM1, PEAR1, PHC1, PHF14, PHF17, PHGDH, PIM1, PKN2, PLXNA4, PLXNC1, PLXND1, POGZ, PPAP2B, PPARGC1A, PPIC, PPP1R12A, PPP1R14A, PPP2R5E, PRDM1, PRKCI, PRKG1, PRMT2, PRRX1, PSAT1, PSD3, PTGDS, PTGIS, PTK7, PTPN13, PTPRD, PYCR1, RAD1, RAD21, RAD23B, RASAL2, RBM17, RBM25, RBM47, RBMS1, RBMS3, REV1, RGS2, RGS4, RGS5, RNASE4, RPS6KA2, RSF1, RSPRY1, RUFY3, RUNX1T1, RUNX2, RYBP, SATB1, SCD, SCML1, SEC14L1, SERPINB9, SERPINF1, SERPINH1,			
						STAU2, STK17B, SULF1, SULF2, SVEP1, SWAP70, SYNCRIP, TANC1, TBX3, TCERG1, TCF4, TCF7L2, TGIF2, TMTC1, TNS3, TOX, TRA2A, TRA2B, TRIM14+G57, TRIM25, TSC22D3, UGCG, USP16, USP18, USP48, VCAM1, VDR, WARS, WASF2, WNK1, XRN2, ZBED1, ZBTB20, ZBTB38, ZFHX3, ZFP91, ZHX2, ZNF148, ZNF22, ZNF24, ZNF462, ZNF711, ZNFX1, ZSCAN31	SETBP1, SETD8, SHMT2, SIX1, SKI, SLC1A3, SLC1A4, SLC25A36, SLC2A12, SLC38A1, SLC38A4, SLC6A9, SLIT3, SLPI, SMAD6, SMARCA1, SMC3, SMC4, SORBS2, SORT1, SOX4, SP110, SPEG, SRSF11, SULF1, SULF2, SYNCRIP, TAF3, TANC1, TBX3, TCEA1, TCEA3, TCEAL7, TCF4, TCF7L1, TCF7L2, TEAD2, TGIF2, THOC2, TMEM176B, TMTC4, TOP1, TOP2A, TOX, TRA2A, TRA2B, TRAM1, TRIB2, TRIB3, TRPS1, TSC22D3, TWIST1, UCHL1, USP13, USP16, USP33, USP34,	Cellular amino acid metabolic process (GO:0006520)	11	23
								Lipid metabolic process (GO:0006629)	27	27
								Nucleobase-containing compound metabolic process (GO:0006139)	147	184

Contd...

Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
							USP48, UTP14C, VCAM1, WARS, WASF1, WASF2, WNK1, XPOT, XRN2, YPEL2, ZAK, ZBED1, ZBTB20, ZBTB38, ZFP36L1, ZHX2, ZNF148, ZNF22, ZNF292, ZNF462, ZNF618, ZNF711, ZNFX1, ZSCAN31	Protein metabolic process (GO:0019538)	110	138
					Sulfur compound metabolic process (GO:0006790)	SULF1, SULF2	CHST11, SLC26A10, SULF1, SULF2	Sulfur compound metabolic process (GO:0006790)	2	4
Multicellular organismal process (GO:0032501)	115	128	15.9	15,1	Single-multicellular organism process (GO:0044707)	ADAM12, ADAM19, ADM, APBB2, BMP1, BNC1, BNC2, CACNA1C, CCDC102B, CDH11, CDH13, CDH6, CDK6, CHRNA9, CNN1, CNN2, CNN3, CNTN3, COL11A1, COL15A1, COL16A1, COL1A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CREB1, CRYAB, CXCR7, DHRS3, ECM2, EDIL3, FBN1, FBN2, FMOD, FNDC3B, FOS, FOXO3, FOXP1, GLI2, GPR124, GPR133, GRIA3, HEPH, HMCN1, HSPB3, HSPB7, HSPG2, HTR2A, ITSN2, JUP, KCNK1, KCNK2, KCNMB1, KLF12, KLF13, KLF9, KRAS, LAMA2, LEPR, LMO7, LPHN2, LRRC17, LRRC3, LUM, MEGF8, MME, MXRA5, MYH10, MYH11, NETO2, NLGN4Y, NRAS, NRP2, NTN1, OMD, OXTR, PALLD, PCDH7, PCDH9, PDE7B, PDGFA, PDGFD, PDLIM1, PHACTR2, POSTN, PPP1R14A, PRRX1, PSD3, RBMS3, RRAS2, S1PR1, SCG5, SEMA3C, SLC1A3, SLIT2, SLITRK6, SNTB1, SNTB2, SORBS2, SPEG, STAU2, SV2A, TAC1, TAGLN, TCF7L2, TENM2, TENM3, TLR3, TPM1, TPM4, VCAM1, WNK1	ADAM12, ADAM19, ADARB1, ADM, ADM2, BMP1, BNC1, BNC2, BOC, CCDC102A, CDH11, CDH13, CDK6, CHRNA1, CNN1, CNN2, CNTNAP1, COL11A1, COL15A1, COL1A1, COL4A1, COL4A2, COL5A1, COL5A2, COL6A1, COL8A2, CREB1, CRYAB, CXCR7, DHRS3, DIRAS3, DUSP1, ECM2, EDIL3, EDNRA, FBN1, FBN2, FMOD, FNDC3B, FOS, FOXC1, FOXO3, FOXP1, FZD4, GLI2, GLI3, GPR124, GPR133, GPR64, GRIA3, GSC, HEPH, HMCN1, HSPB3, HSPG2, HTR2A, HTR2B, ITSN2, JUP, KCNK1, KCNK2, KLF12, KLF13, KLF9, KRAS, LAMA2, LEPR, LIN7A, LPHN2, LRIG3, LRRC17, LUM, MEGF8, MME, MXRA5, MYH10, MYH11, MYL9, NRP2, NTN1, OBSL1, OMD, OSR2, OXTR, PALLD, PCDH7, PCOLCE, PDE4B, PDE4D, PDE7B, PDGFA, PDGFD, PDLIM1, POSTN, PPP1R14A, PRRX1, PSD3, PTGIS, RASD1, RBM47, RBMS3, RIMS3, S1PR1, SCG5, SEMA3C, SEMA3D, SESTD1, SLC1A3, SLC1A4, SLC6A9, SLIT3, SMO, SNTB1, SNTB2, SORBS2, SPEG, SV2A, TAGLN, TCF7L1, TCF7L2, TENM2, TENM3, TLR3, TPM1, TRPC6, VCAM1, WNK1, WNT5A	Single-multicellular organism process (GO:0044707)	115	128

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
Reproduction (GO:0000003)	24	35	3.3	4,1	Fertilization (GO:0009566)	ADAM12, ADAM19, ADAMTS1, CRISPLD2, GLIPR2, VWCE	ADAM12, ADAM19, ADAMTS1, CRISPLD1, CRISPLD2, VWCE	Fertilization (GO:0009566)	6	6
					Gamete generation (GO:0007276)	AKT3, BMP4, CCNJL, CRISPLD2, GDF5, GLIPR2, GPR124, GPR133, INHBA, INHBE, JUP, KDM4B, LPHN2, MAGED4, NDN, STAU2, TCF4, TGFB2, USP48, ZFHX3	ADARB1, BMP4, C1R, CCNJL, CFD, CRISPLD1, CRISPLD2, FHL1, GPR124, GPR133, GPR64, INHBA, INHBE, JUP, KDM4A, KDM4B, KDM5A, LMO4, LPHN2, MAGED4, NDN, TCF4, TGFB2, TGFB3, USP13, USP33, USP34, USP48	Female gamete generation (GO:0007292)	7	7
								Spermatogenesis (GO:0007283)	8	11
Response to stimulus (GO:0050896)	98	99	13.6	11,7	Cellular defense response (GO:0006968)	CXCL1, CXCL10, CXCL6, ELF1, ETV6, ETV7, FLI1, IFI35, LOX, NMI, PHLDB2, STAT1, STAT2, TNFSF10, ULBP1, ZFHX3	CXCL6, ELF1, ELF2, ETV6, FHL1, FLI1, IL20RB, LMO4, LOX, PHLDB2, SESTD1, ULBP1	Cellular defense response (GO:0006968)	16	12
					Immune response (GO:0006955)	C1QTNF5, CCL2, CCL7, CCL8, CEBPD, CXCL1, CXCL10, CXCL6, CXCR7, ELF1, ETV6, ETV7, FLI1, GBP1, GBP2, GBP5, GHR, GPR124, GPR133, IFI16, IFI35, IL6ST, IL7R, IRF7, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, LEPR, LPHN2, NMI, OAS1, OAS2, OAS3, PAPPA, PHLDB2, STAT1, STAT2, STAU2, SVEP1, SWAP70, TAC1, TNFAIP2, TNFSF10, TRIM14, ULBP1	ADARB1, C1QTNF5, C1R, CCL11, CCL2, CCL7, CCL8, CFB, CXCL6, CXCR7, ELF1, ELF2, ETV6, FLI1, GBP1, GBP5, GPR124, GPR133, GPR64, IFI16, IL11RA, IL20RB, IL6ST, KLF12, KLF13, KLF2, KLF6, KLF7, KLF9, LEPR, LPHN2, PAPPA, PHLDB2, SESTD1, TNFAIP2, ULBP1	B cell-mediated immunity (GO:0019724)	16	16
								Complement activation (GO:0006956)	3	4
								Natural killer cell activation (GO:0030101)	2	1
								Response to interferon-gamma (GO:0034341)	9	4
					Response to endogenous stimulus (GO:0009719)	FOXO3, SKI	FOXO3, SKI	Response to endogenous stimulus (GO:0009719)	2	2
					Response to external stimulus (GO:0009605)	ANGPT1, BMP1, COL12A1, COL14A1, CXCL1, CXCL6, EDIL3, HEPH, ITGB8, ITGBL1, NETO2, NRP2, PAPPA, PDGFD, PLSCR1, SVEP1, VIT	ANGPT1, BMP1, C1R, CFB, CFD, CNTNAP1, COL12A1, COL14A1, CXCL6, EDIL3, HEPH, IL20RB, ITGB8, ITGBL1, NRP2, PAPPA, PCOLCE, PDGFD, VIT	Blood coagulation (GO:0007596)	15	18

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Appendix Table 2: Contd...

Biological process (downregulated)	Number of genes		Percent of gene hit against total		Subgroups of biological process	Genes		Subgroups of biological process	Number of genes	
	1 day	7 days	1 day	7 days		1 day	7 days		1 day	7 days
					Response to stress (GO:0006950)	CEBPD, CREB1, CRYAB, EIF2AK2, FOXO3, GADD45B, GPR124, GPR133, HSP90B1, HSPB3, HSPB7, HSPH1, LPHN2, MSRB3, NFE2L2, NFE2L3, NR4A1, PDGFA, SMAD6, STK17B	CEBPG, CREB1, CRYAB, EDNRA, FOXO3, GPR124, GPR133, GPR64, GPX7, HSP90B1, HSPA5, HSPB3, LPHN2, MKNK2, MOCOS, MSRB3, NFE2L1, NFE2L2, NFE2L3, NR4A1, NR4A3, PDGFA, SMAD6, ZAK	Response to stress (GO:0006950)	20	24
					Response to toxic substance (GO:0009636)	CLIC4, MEST	CLIC3, CLIC4, GPX7, MEST	Response to toxic substance (GO:0009636)	2	4